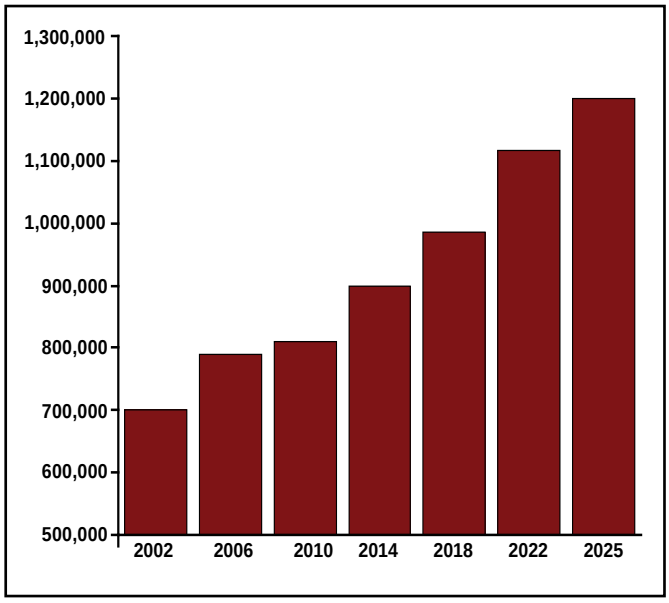
enhanced outcomes that are produced by self-expanding stents for recanalization of acute cerebrovascular occlusions compared with other means of thrombolysis, the FDA approved the SAIS (Stent-Assisted recanalization in acute Ischemic Stroke) study.

Figure 1. Projected Number of Strokes in the US: 2002–2025.



Eligibility included age ≥18 years and presentation within 8 hours of stroke onset. Subjects were required to have an NIHSS ≥8, angiographic demonstration of focal intracerebral artery occlusion not >14 mm, and either contraindication to IV tPA or failure to improve 1 hour after tPA administration. Patients who had CT perfusion imaging that demonstrated >1/3 at-risk territory with nonsalvageable brain or with an intracerebral hemorrhage were excluded. More than 50% of the patients were female, mean age was 63±18 years, mean NIHSS score=14±3.8, and 85% had thrombolysis in myocardial infarction (TIMI)* scores=0.

All 20 patients achieved recanalization; 60% achieved a TIMI score=3 (full flow restored) and 40% had a TIMI score=2 ($p<0.0001$ compared with presenting TIMI scores). Improvement in NIHSS was documented in 85% of patients, wherein 65% improved by ≥4 NIHSS points. Median NIHSS improvement from intervention to discharge was 9 (range -6 to 14; $p<0.001$). There were 5 (25%) deaths at 1 month, which compares well with other similar studies. Dr Mocco completed his presentation with a case study of a 65-year-old male with stroke onset 6 hours before presentation and an NIHSS score of 14. Recanalization was achieved in 24 minutes. Four hours after the procedure, the patient's NIHSS score was 0. Based on these data, the FDA has approved an additional 20-patient extension to continue this prospective study, with the movement toward a definitive trial on the horizon.

*In this case, TIMI represents the degree of occlusion.

Results of a Randomized, Multi-Center Safety Trial of Perflutren Lipid Microspheres: TUCSON

Microspheres that are combined with systemic tPA and rational transcranial Doppler (TCD) show promise as a recanalization tool in patients with acute ischemic stroke if administered within 3 hours of stroke onset. Carlos A. Molina, MD, Vall d'Hebron Hospital, Barcelona, Spain, reported results from the Transcranial Ultrasound in Clinical SONolyis (TUCSON; NCT00504842) trial, identifying 1.4 mL of MRX-801 perflutren lipid microspheres (μS) as a safe dose that produces higher rates of recanalization (67% vs 33%; $p=0.22$) compared with controls.

Earlier studies have shown that TCD can safely enhance the thrombolytic activity of tPA and increase the rates of recanalization and stroke recovery [Alexandrov AV et al. *New Engl J Med* 2004]. When combined with microbubbles [Molina CA et al. *Stroke* 2006] or microspheres [Alexandrov AV et al. *Stroke* 2008], complete, sustained recanalization and clinical recovery rates are even higher. The ultrasonography transiently expands the microspheres, transmitting energy momentum to the surrounding fluids, thereby furthering the process of recanalization of blocked vessels.

The TUCSON study [Barreto AD et al. *Int J Stroke* 2009] enrolled 35 acute (<3 hours) ischemic stroke patients with proximal intracranial arterial occlusions. Cohort 1 (n=12) received IV-tPA + continuous 2-MHZ TCD + 1.4 mL μS, Cohort 2 (n=11) received IV-tPA + continuous 2-MHZ TCD + 2.8 mL μS, and controls (n=12) received IV-tPA + intermittent 2-MHZ TCD. Infusion was over a 90-minute period.

At baseline, the mean age in all groups was ~65 years, mean NIHSS was ~13, and mean blood pressure was ~153/77 mm Hg. Approximately 23% of patients had grade 0-1 thrombolysis in brain ischemia (TIBI), and 77% presented with M1 middle cerebral artery occlusions.

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