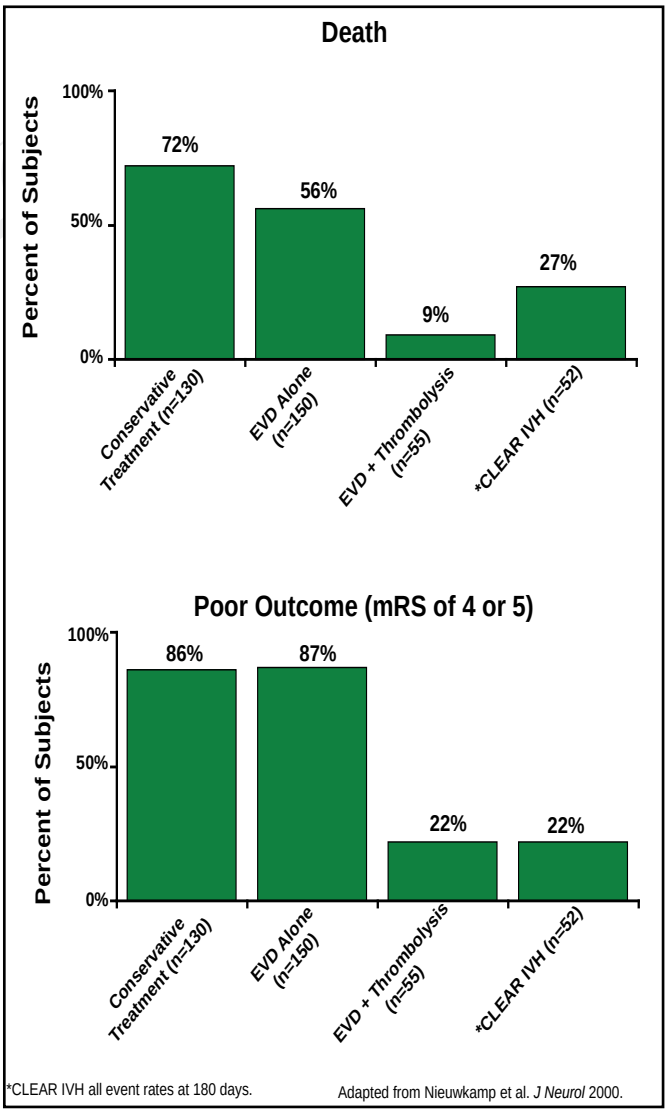
were as follows: 17 patients had mRS scores between 0-3 (0=no disability; 3=moderate disability); average Barthel score=93.8; average NIHSS=1.17 (0 indicates normal); and GOS=1.17 (1 indicated good recovery). Overall, these patients were highly functional as indicated by these scales. Those patients (n=13) who scored 0 to 3 on the mRS also demonstrated good daily functionality as measured by the Stroke Impact Scale (SIS-16), validating the mRS measurements. Five patients were totally normal. By 180 days, 27% (14/52) of the patients had died and 22% (11/15) were rated as having poor outcomes (mRS of 4 or 5). The effect of rt-PA on good clinical outcome at 30 days (mRS 0-4) had an OR of 0.24 (Figure 1).

Figure 1. CLEAR IVH All Event Rates at 180 Days.



*CLEAR IVH all event rates at 180 days.

Adapted from Nieuwkamp et al. *J Neurol* 2000.

The positive findings from this study will allow the authors to proceed to a CLEAR Phase III trial, which has a projected enrollment of 500 patients at 50 to 70 worldwide sites that have neurosurgical and stroke expertise. The hypothesis that is to be tested in this placebo-controlled, blinded, randomized trial is whether EVD plus rt-PA treatment of IVH obstruction in the third and fourth ventricles will increase the percentage of patients in the mRS 0 to 3 group compared with EVD alone.

Final Results of an FDA-approved Prospective, Multicenter, Single-arm Trial of Stent-Assisted Recanalization for Acute Ischemic Stroke

Results from an FDA-approved, prospective pilot trial that were presented by J. Duffy Mocco, MD, University of Buffalo Neurosurgery, Buffalo, NY, suggest that the use of a self-expanding, intracranial stent for acute stroke may achieve high levels of revascularization. This follows on the heels of the Mechanical Embolus Removal in Cerebral Ischemia (MERCI; NCT00318071) trials that reported recanalization rates that ranged from approximately 60% to 70% percent with low associated morbidity.

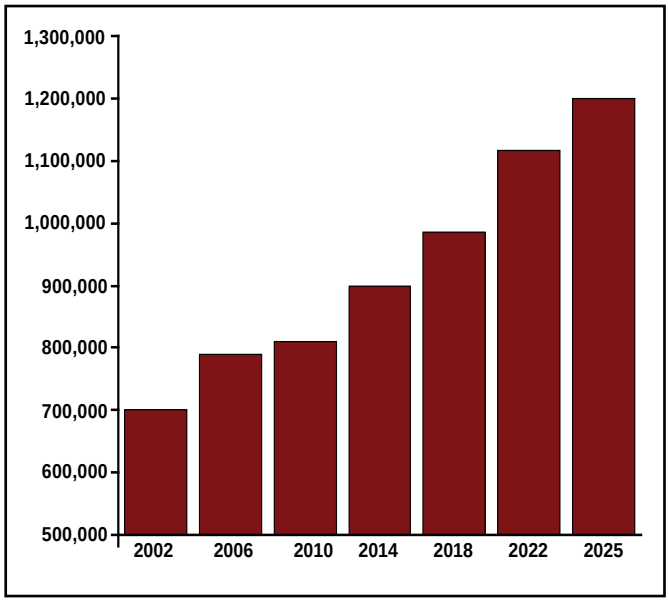
Stroke is a leading cause of long-term disability and the third-leading cause of death. It is estimated that 795,000 strokes occur each year in the United States. This number is projected to increase 40% by the year 2025 (Figure 1). The MERCI 1 [Gobin YP et al. *Stroke* 2004] and Multi MERCI [Flint AC et al. *Stroke* 2007] trials, which used the MERCI Retrieval System, compared outcomes in patients who received mechanical embolectomy (recanalization) with outcomes in patients who were not recanalized. Significantly improved clinical outcomes and reduced mortality were reported for the recanalized patient group.

Although mechanical recanalization appears to work, there are patients for whom the MERCI device fails. Based on the results of this pilot study, Dr. Mocco said he believes that the use of intracranial stenting for acute ischemic stroke after failed thrombolysis with other means is now possible.

Based on preliminary results [Levy EI et al. *Neurosurgery* 2006; Zaideat OO et al. *Stroke* 2008] that have demonstrated

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.