were a total of 3 ischemic strokes within 1 year (7.5%). Two patients had minor strokes that resolved completely. One patient had a major (mRS 4) stroke.

## The Results of NEST-2: A Double-Blind, Randomized, Phase III Study Evaluating the Safety and Efficacy of Transcranial Laser Therapy for Acute Ischemic Stroke within 24 Hours of Stroke Onset

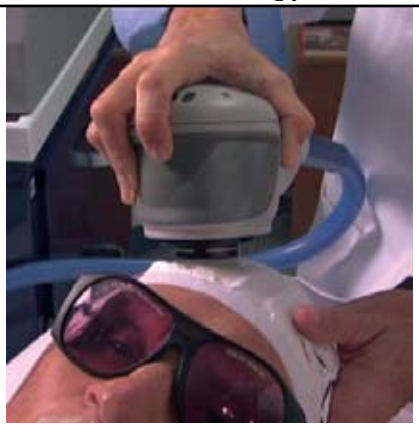
Results from the NeuroThera® Effectiveness and Safety Trial-2 (NEST-2; NCT00419705) show no difference in efficacy between transcranial laser therapy (TLT) and sham treatment for the treatment of acute ischemic stroke (AIS) when applied within 24 hours of diagnosis.

The NeuroThera® Effectiveness and Safety Trial-2 (NEST-2) was a phase III prospective, double-blind, randomized, sham-controlled, multicenter (n=58) study of TLT for the treatment of AIS. The study population included subjects, aged 40 to 90 years, with an NIHSS score of 7 to 22 who were diagnosed with AIS. Evidence of intracranial, subdural, or subarachnoid hemorrhage was cause for exclusion, as were prestroke mRS score ≥3; blood glucose >400 mg/dl or <60 mg/dl; and sustained systolic blood pressure (BP) >190 mm Hg or <80 mm Hg, or diastolic >110 mm Hg or <50 mm Hg. Subjects who had received thrombolytic therapy (tPA) and those with head implant (eg, clipped aneurysm, Hakim valve) also were excluded. Subjects were followed for 90 days.

The primary efficacy endpoint was a modified Rankin Scale (mRS) score of ≤2 at 90 days. Secondary endpoints were the shift in mRS score and NIHSS score 0 or 1 at 90 days *or* an improvement of ≥9 points. Safety endpoints included mortality, adverse events, and intracerebral hemorrhage.

Subjects were randomly assigned to receive TLT (n=331) or sham treatment (n=327). Treatment was performed at 20 locations for 2 minutes each. For patient comfort and to avoid breaking the blind, the lens was mildly refrigerated. Median NIHSS score at baseline was 12 in the treatment group and 13 in the sham group. Mean time to treatment was approximately 14 hours in both groups (Figure 1).

**Figure 1. Transcranial Laser Therapy with NeuroThera®.**



*Subject presented is actor and not actual patient

- **20 locations for 2 minutes each**
- **Treatment regimen is the same regardless of stroke location**
- **808 nm wavelength is infrared and invisible**
- **Power 10 mW/cm$^2$**
- **Lens is mildly refrigerated for patient comfort and blinding**

**NeuroThera® System is Limited by Federal Law to Investigational Use Only**

There was no difference in the primary outcome of mRS score ≤2 (36.3% in the TLT group and 30.9% in the sham group; p=0.094). Adverse events were similar in both groups (Table 1). The shift in mRS score in the treatment group was equal to or better than in the sham population for mRS 0-4; however, there was no difference at the upper end of the score (mRS 5,6).

**Table 1. Safety Results.**

| | TLT (n=331) | Sham (n=327) |
|---|---|---|
| **90 day mortality** | 17.5% | 17.4% |
| **Serious adverse events** | 37.8% | 41.8% |
| **Intracerebral hemorrhage** | 14.8% | 17.1% |
| **Nervous system disorders** | 15.4% | 15.5% |
| **Respiratory disorders** | 10.6% | 9.8% |
| **Infections** | 7.6% | 9.5% |
| **Cardiac disorders** | 6.6% | 7.9% |

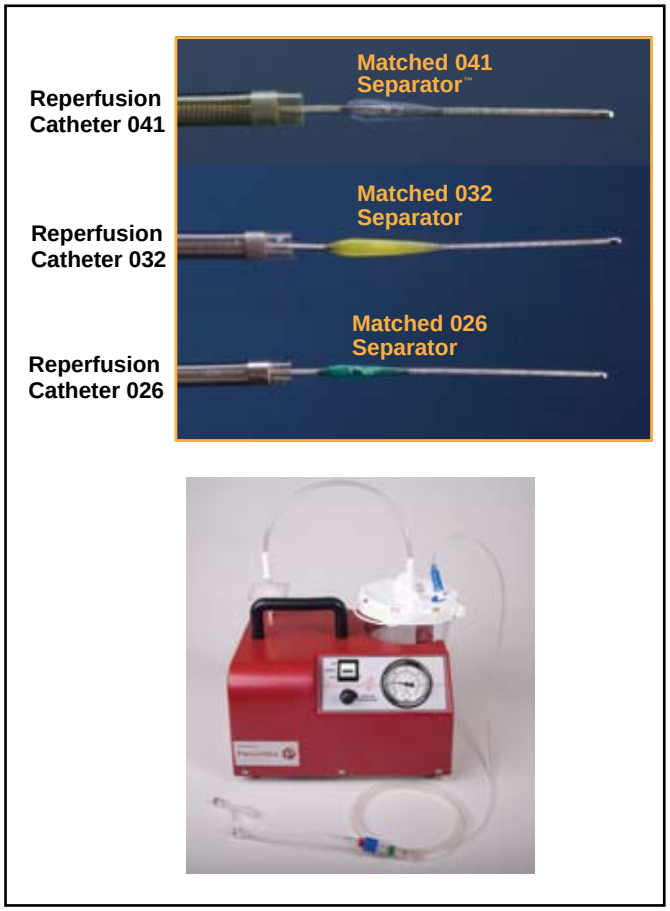
TLT is apparently safe and well tolerated, with no important effect of time from onset to treatment within the 24-hour time window. Although there was no difference in efficacy in the overall population, results from a prespecified subset of 434 patients with mRS 7 to 15 showed a significant (p=0.044) treatment effect in 51.6% of TLT patients versus 41.9% of patients in the sham group. "In light of the demonstrated safety of TLT, the results of this post hoc analysis are promising," said Justin Zivin, MD, San Diego VA Medical Center, San Diego, CA, "as they may indicate a benefit for patients who suffer moderate to moderately severe stroke." A multinational phase III study is planned (NEST-3).

## Initial Post-Market Experience of the Penumbra System: Revascularization of Large Vessel Occlusion in Acute Ischemic Stroke in the United States and Europe

The Penumbra System is a mechanical clot removal device that is indicated for the revascularization of occluded large vessels in acute ischemic stroke (AIS). It has been approved for commercial use in the United States and Europe. In a postmarket study to assess its safety and effectiveness in a "real world" setting, the performance of the device was deemed to be comparable with the results of the pivotal Penumbra trial with regard to revascularization rate, incidence of adverse events, intracerebral hemorrhage (ICH), all-cause mortality, and 90-day good functional outcome.

The Penumbra System consists of a reperfusion catheter that is optimized for navigation and aspiration and a separator that cleans and clears clots from the occluded vessel (Figure 1). This was a retrospective case review study of 139 patients who were treated with the device at 7 centers. The primary endpoints were the rate of revascularization of the target vessel (TIMI 2 or 3) and procedural serious adverse events (SAEs). Secondary endpoints included percentage of patients with modified Rankin Score (mRS) ≤2 at 90 days, symptomatic ICH (sICH), and all-cause mortality. Eligible patients had an NIHSS score >8, symptom onset within 8 hours, and TIMI score of 0 or 1 at presentation.

**Figure 1. Penumbra Aspiration System.**




Mean age of the patient population (72 men and 67 women) was 64±15 years. Mean NIHSS score was 16±6. Target vessels included 26% internal carotid artery (ICA), 51% middle cerebral artery (MCA), and 24% vertebrobasilar artery. This compared with 18% ICA, 70% MCA, and 8% vertebrobasilar artery in the pivotal trial. Arterial puncture was initiated within 4.5 hours from symptom onset, and mean time for revascularization was 48 minutes, similar to that in the pivotal trial.

After use of the Penumbra System, 84% of the treated vessels were revascularized to TIMI 2 or 3. ICH rates at 24 hours were 5.8% and 7.2% for asymptomatic ICH and symptomatic ICH, respectively, which were lower, but not significantly, compared with those in the pivotal trial. There were a total of 8 SAEs and 2 device malfunctions (none of which resulted in patient injury). All-cause mortality was 22% (31/139). At discharge, 34% of the patients had a ≥10 point NIHSS improvement or NIHSS score 0-1. Of the patients who had reached the 90-day follow-up, 40% had a mRS ≤2.