214 The Field Administration of Stroke Therapy - Magnesium (FAST-MAG) Phase 3 Trial: Primary Results

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BACKGROUND: Magnesium is neuroprotective in preclinical models of stroke and has been safe and shown signals of potential efficacy when delivered early after onset of human cerebral ischemia. Delayed initiation of neuroprotective agents has hindered past neuroprotective agent trials. We performed a multicenter, randomized, double-blind, placebo-controlled phase 3, trial to test whether paramedic initiation of intravenous magnesium sulfate within 2 hours of symptom onset improves the longterm functional outcome of hyperacute stroke patients.

METHODS: Inclusion criteria were: 1) likely stroke as identified by the Los Angeles Prehospital Stroke Screen (LAPSS), 2) age 40-95, 3) symptom onset within 2 hours of treatment initiation, 4) deficit present ≥ 15 minutes. Trial sites included 315 ambulances, 40 EMS agencies, and 60 receiving hospitals throughout Los Angeles and Orange Counties, with 2988 paramedics trained in study procedures. From Jan 2005 - Dec 2012, paramedics in the field administered a loading dose (4 grams over 15 minutes) of magnesium sulfate (Mg) or matched saline placebo. Upon arrival in an ED, a maintenance infusion followed: 16 grams Mg or matched placebo over 24 hours. The primary endpoint was the modified Rankin Scale measure of global disability at 90 days.

RESULTS: Among the 1700 enrolled patients, mean age was 69 (SD 13.6), 42.7% were female, median pretreatment stroke severity on the Los Angeles Motor Scale (LAMS) was 4.0, and median early post-treatment NIHSS stroke severity on ED arrival was 9.0. Final diagnosis of the presenting event was acute cerebral ischemia in 73.0%, acute hemorrhagic stroke in 23.2%, and stroke-mimicking condition in 3.8%. The median time from last known well to start of study infusion was 48 minutes (IQR 37 - 68). The proportion of patients receiving study infusion within the first hour after last known well was 74.1%. CONCLUSION: Prehospital initiation of neuroprotective agents can be performed in a large phase 3 acute stroke trial, permitting rapid drug start, with treatment in the first, “golden” hour in three-quarters of patients. The study blind will be broken in late fall and the first public presentation of trial efficacy results presented at the ISC meeting.