

Collateral Advantages:
The Secondary Gain from
Clinical Trial Implementation

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Stroke and the Golden Hour



- Narrow therapeutic time window
- Early intervention critical for stroke care
- 35-70% of stroke patients arrive by ambulance

Trials of Neuroprotective Agents for Stroke, 1955-2000

Neuroprotective agents tested	49
RCTs performed	114
Patients enrolled	21,445
Neuroprotective agents approved	0

Time windows: 4-48 hours

-- Kidwell, Liebeskind, Starkman, Saver, Stroke 2001

The Field Administration of Stroke Therapy - Magnesium (FAST-MAG) Phase 3 Trial



JL Saver, M Eckstein, S Stratton, F Pratt, S Hamilton, R Conwit, D Liebeskind, P Lyden, N Sanossian, G Sung, I Kramer, G Moreau, R Goldweber, S Starkman, for the FAST-MAG Investigators and Coordinators

Supported by NIH-NINDS



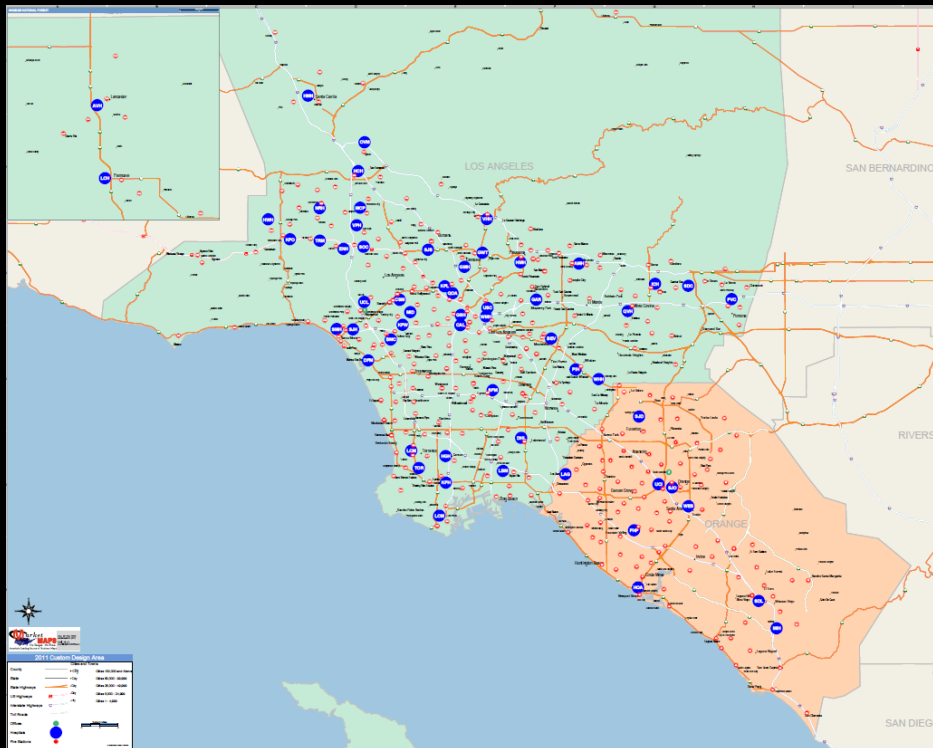
Aims

- Specific Aim: To demonstrate that paramedic initiation of the neuroprotective agent magnesium sulfate in the field is an efficacious and safe treatment for acute stroke
- Systems Aim: To demonstrate that field enrollment and treatment of acute stroke patients is a practical and feasible strategy for pivotal phase 3 stroke trials

Design

- Placebo-controlled, double-blind, randomized
- Multicenter, single region, Los Angeles County and Orange County
- Mg 4 gm field x 15 min, 16 gm maintenance x 24h
- 1700 patients, all within 2 hours of onset
- NIH-NINDS supported (\$16 million over 8 years)
- Jan 2005-Mar 2013
- Primary endpoint: 90 day stroke disability (Rankin Scale)

FAST-MAG Trial Consortium



Performance Sites in Los Angeles and Orange Counties

- Los Angeles and Orange Counties
 - » Population 13.3 million
- 40 EMS Provider Agencies
 - » 315 ambulances
 - » 2988 paramedics
- 60 receiving hospitals

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Entry Criteria

Inclusion

- Suspected stroke identified by the Los Angeles Prehospital Stroke Screen (LAPSS)
- Age 40-95, inclusive
- Last known well time within 2h of treatment initiation
- Deficit present for ≥ 15 minutes

Results

Supported by NIH-NINDS



ORIGINAL ARTICLE

Prehospital Use of Magnesium Sulfate as Neuroprotection in Acute Stroke

Jeffrey L. Saver, M.D., Sidney Starkman, M.D., Marc Eckstein, M.D., Samuel J. Stratton, M.D., Franklin D. Pratt, M.D., M.P.H.T.M., Scott Hamilton, Ph.D., Robin Conwit, M.D., David S. Liebeskind, M.D., Gene Sung, M.D., Ian Kramer, M.D., Gary Moreau, M.D., Robert Goldweber, M.D., and Nerses Sanossian, M.D.,
for the FAST-MAG Investigators and Coordinators*

- No difference in disability or mortality at 3 months between MAG group vs. placebo

Supported by NIH-NINDS



Collateral Advantages

- First prehospital stroke phase 3 RCT
- Demonstrated accuracy of paramedic identification of acute stroke (stroke mimics 3.9%)
- First “golden hour” (<1 hr) stroke phase 3 trial
 - » Over 75% treated within 60 min. of last known well time
- Development of Acute Stroke Centers in Los Angeles
- Increased rate of tPA administration (2% to 37%)
- Provided foundation for future prehospital RCTs
- Leading to creation of Comprehensive Stroke Centers



Failed to show benefit of magnesium as neuroprotective agent in acute stroke... but DID result in significant **COLLATERAL ADVANTAGES** for both enrolled and future stroke patients!

