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

- Los Angeles and Orange Counties
  » Population 13.3 million
- 40 EMS Provider Agencies
  » 315 ambulances
  » 2988 paramedics
- 60 receiving hospitals
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 $\geq 15$ minutes
Results
Prehospital Use of Magnesium Sulfate as Neuroprotection in Acute Stroke

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

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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

Supported by NIH-NINDS
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!