Treat Stroke in the Field: Lessons from the NIH FAST-MAG Trial

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Professor of Neurology
Director, UCLA Stroke Center
Disclosures and Support

• Disclosures
  » UC Regents receive payment for SAB: Talecris, Covidien, CoAxia, St. Jude Medical
  » UC Regents receive payments for enrolled patients: NIH CLEAR-ER, IMS 3, MR RESCUE Trials, Lundbeck
  » UC Regents hold patent rights in the Merci Retriever
  » Have declined Genentech honoraria since 2002

• Support
  » Supported in part by National Institute of Health and American Heart/American Stroke Association
The Ischemic Penumbra

Core Infarct

Ischemic Penumbra: zone of salvageable tissue surrounding core infarct
In a typical acute ischemic stroke, every minute the brain loses:

- 1.9 million neurons
- 14 billion synapses
- 7.5 miles myelinated fibers

-- Saver, Stroke 2006
Onset to Treatment Time for IV TPA and Odds of Excellent Outcome

- Pooled, patient level analysis
- 8 trials
  - NINDS 1 and 2
  - ATLANTIS A and B
  - ECASS 1, 2, and 3
  - EPITHET
- 3670 patients

--Saver + Levine, Lancet 2010
Minutes Matter

- Every 10 minutes delay, 1 fewer of 100 patients treated benefits from IV tPA

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--Saver, Stroke, In Press
IV TPA Under 3 Hours – Patient Education

• Joint AHA-AAN-ACEP text tool to educate patients and families
• UCLA icon array tool based on AHA-AAN-ACEP
  » Available for free use under Creative Commons license

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Stroke and the Golden Hour

- Narrow therapeutic time window
- Early intervention critical for stroke care
- Prehospital personnel
  - 35-70% of stroke patients arrive by ambulance
  - Unique position: first medical professional to come in contact with stroke patient

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Emergent Stroke Care and the Chain of Survival

Patient Knowledge
Calling 911
EMS System
ED Staff
Stroke Team
Stroke Unit
Prehospital Stroke Recognition: Applications

- **Widespread**
  - Optimize rapid transport ("Scoop and go")
  - Pre-arrival notification
    - Radio alert receiving hospital
    - Activate stroke team
    - Clear head CT/MR scanner
  - Diversion to stroke critical care centers

- **Emerging**
  - Differential diversion to comprehensive vs primary stroke centers
  - Active treatment in the field – neuroprotectives, lytics, antihypertensives
Prehospital Stroke Identification in the 1990s

- Paramedics in San Francisco:
  » recognized 57% of acute stroke patients

- Paramedics in Cincinnati:
  » recognized 72% of acute strokes
Selected Approaches to Improving EMS Prehospital Stroke Recognition

- Los Angeles Prehospital Stroke Screen (LAPSS)* **
- Cincinnati Prehospital Stroke Scale (CPSS)*
- Face Arm Speech Test**
- Paramedic Quick Screen (San Diego)
- Miami Evaluation of Neurologic Deficit (MEND)
- UAB Stroke Observational Scale (SOS)
- Maryland Tele-BAT

*Endorsed in ACLS Cardiopulmonary Resuscitation Guidelines, Circulation 2000
**Prospectively validated in field testing
LAPSS
Los Angeles Prehospital Stroke Screen
LAPSS Design

- **History (4 items)**
  - onset/duration of symptoms
  - age
  - history of seizure disorder
  - baseline functional status

- **Exam (3 items): identifies unilateral weakness**
  - facial weakness
  - arm drift
  - grip strength

- **Fingerstick blood glucose (1 item)**
Motor Deficits in Acute Stroke

- LAPSS and CPSS emphasize motor deficits:
  - Present in 83-90% of all strokes
  - Major determinant of long-term disability
  - Testing performed reliably and briefly by health personnel not specifically trained in neurology
Results - 1298 Runs

- Neurologically Relevant Hx: n=410 (32%)
- Final Dx Stroke: n=36 (3%)
- Non-Neurologically Relevant Hx: n=852 (65%)
## Results: Instrument Performance

**LAPSS Completed Runs (Neuro Sx Runs)**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>91%</td>
<td>(76-98%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>99%</td>
<td>(97-99%)</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>97%</td>
<td>(84-99%)</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>98%</td>
<td>(96-99%)</td>
</tr>
</tbody>
</table>
Prehospital Stroke Management

- **Perform**
  - Determine and document time of onset
  - Initiate cardiac monitoring
  - Insert intravenous line
  - Perform serum glucose measure
  - Administer oxygen
  - Notify ED quickly
  - Transport as soon as possible (“scoop and go”)

- **Avoid**
  - Delay transport
  - Give large volumes of fluid
  - Give dextrose (unless hypoglycemic)
Stroke Systems: Two Tier US Model

- **EMS**
  - Trained dispatchers, high priority triage
  - Paramedics trained in stroke recognition (e.g. LAPSS)
  - Deliver patients to nearest stroke capable hospital
  - Pre-arrival notification

- **Spokes**
  - Primary Stroke Centers
    - Able to provide initial, ED care
    - Able to use rt-PA and other acute therapies in a safe and efficient manner
    - Have Stroke Units and can admit patients
  - Stroke Ready Hospitals
    - Able to provide initial, ED care, often via telemedicine
    - Able to use rt-PA and other acute therapies safely and efficiently

- **Hubs**
  - Comprehensive Stroke Centers
    - Able to care for complex patients
    - Advanced treatments (i.e. coils, stents, IA recanalization, etc)
    - Trained specialists in key areas (Vascular neurology, Neurointerventional procedures, Neurocritical Care, Vascular Neurosurgery)
### Stroke Center Diversion: Houston Experience

Wojner et al, Stroke 2004

- 6 designated stroke centers
- EMS / Stroke Center / Consumer interventions
- Paramedic training, modified LAPSS

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts/mo stroke centers</td>
<td>62</td>
<td>91</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Proportion of citywide</td>
<td>59.6%</td>
<td>68.7%</td>
<td></td>
</tr>
<tr>
<td>Paramedic dx sensitivity</td>
<td>66%</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>Paramedic dx specificity</td>
<td>98%</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td>IV TPA rate</td>
<td>7.1%</td>
<td>11.3%</td>
<td>.042</td>
</tr>
</tbody>
</table>
Primary Stroke Centers in the United States

Certified as of May 2010

Joint Commission 708
HFAP (Osteopathic) 15
Dept of Health/EMS 290
Total ~950

All as of September 2012

GWTG – Stroke 1,641
National Access to Primary Stroke Centers

<table>
<thead>
<tr>
<th>Travel Time</th>
<th>Ground Ambulance</th>
<th>Ground + Air Ambulance</th>
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<tbody>
<tr>
<td>30 mins</td>
<td>22%</td>
<td>26%</td>
</tr>
<tr>
<td>45 mins</td>
<td>43%</td>
<td>66%</td>
</tr>
<tr>
<td>60 mins</td>
<td>55%</td>
<td>79%</td>
</tr>
</tbody>
</table>

--Albright et al, Arch Neurol 2010
Dissemination of Preferential EMS Routing to PSCs
--Song and Saver, Stroke 2012
Primary Stroke Center Coverage of US Population in 2010

17 states, multiple additional counties, 53% US population

- States
  - Connecticut
  - Delaware
  - Florida
  - Georgia
  - Illinois
  - Maryland
  - Massachusetts
  - Missouri
  - New Jersey
  - New York
  - North Carolina
  - North Dakota
  - Oklahoma
  - Rhode Island
  - Texas
  - Utah
  - Virginia
  - Washington

- Counties
  - Alabama
    - 7 counties
  - Arizona
    - Maricopa-Phoenix
  - California (16 of 58)
    - Alameda
    - Butte
    - Colusa
    - Kern
    - Los Angeles
    - Nevada
    - Orange
    - Placer
    - Sacramento
    - San Diego
    - San Francisco
    - San Mateo
    - Santa Clara
    - Sutter
    - Yolo
    - Yuba
Primary Stroke Center Coverage of US Population in 2010

- Live in jurisdictions with direct routing to Stroke Centers
  - 157 million Americans
  - 53% of US population
- Live in jurisdictions with routing to nearest hospital, not PSCs
  - 147 million Americans
  - 47% of US population
Select Prehospital Stroke Treatment Strategies Currently in Clinical Trials

- **Thrombolysis**
  - Homburg Trial
  - PHANTOM – S, Berlin

- **Blood Pressure Control**
  - For diverse patients
    - RIGHT trial, glycercyl trinitrate
    - PIL-FAST trial, Lisinopril
  - For severely hypertensive patients
    - FAST-BP, glycercyl trinitrate

- **Neuroprotection**
  - Remote ischemic perconditioning
    - Danish trial, phase 2B
    - FAST-TRIP, phase 2
  - Magnesium
    - FAST-MAG, phase 3
Mobile Stroke Units for Prehospital Thrombolysis

--Walter et al, PLOS One, 2010, Homburg

--Audebert et al, Berlin
## Randomized Trial of Prehospital vs ED Lytic Initiation

|                                | Prehospital Lysis  
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td></td>
<td>(n = 53)</td>
</tr>
<tr>
<td>Alarm to decision</td>
<td>35 min</td>
</tr>
<tr>
<td>Onset to decision</td>
<td>56 min</td>
</tr>
<tr>
<td># TPA Treated</td>
<td>12</td>
</tr>
<tr>
<td>Alarm to treatment</td>
<td>38 min</td>
</tr>
<tr>
<td>Onset to treatment</td>
<td>72 min</td>
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<tr>
<td></td>
<td>Hospital Lysis</td>
</tr>
<tr>
<td></td>
<td>(n=47)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>Alarm to decision</td>
<td>76 min</td>
</tr>
<tr>
<td>Onset to decision</td>
<td>104 min</td>
</tr>
<tr>
<td># TPA Treated</td>
<td>8</td>
</tr>
<tr>
<td>Alarm to treatment</td>
<td>73 min</td>
</tr>
<tr>
<td>Onset to treatment</td>
<td>153 min</td>
</tr>
</tbody>
</table>

No difference efficacy or safety outcomes

Elevated Prehospital BP Predicts Further Worsening in ICH

- Field BP higher among ICH (176/100 v 156/87)
- Initial GCS in ICH 15 (IQR 15-15) v 15 (IQR 14-15), p=0.018
- Deterioration in 30% vs. 6% (p<0.0001)
- In ICH higher SBP in deterioration (SBP 182 v 173, p=0.022)
  - Deterioration increased with quartile SBP
    - 1\textsuperscript{st} 20%, 2\textsuperscript{nd} 27%, 3\textsuperscript{rd} 28%, 4\textsuperscript{th} 38%, p=0.045
    - Odds of deterioration increased in each SBP quartile
      - Relative to the 1\textsuperscript{st}: OR 1.5 (95%CI 0.58, 3.7) for 2\textsuperscript{nd}, 1.6 (0.63, 3.9) for 3\textsuperscript{rd}, OR 2.5 (1.02, 6.09) for 4\textsuperscript{th}
- In cerebral ischemia, BP was not related to ECD: SBP 158 vs. 156, DBP 87 vs. 8

--Sanossian, Starkman, Liebeskind, et al. *Cerebrovascular Diseases* 31(S2) 73, 2011
**INTERACT1: Reduction in *absolute* hematoma growth over 72 hours according to time from onset to treatment**

---Arima et al, Stroke 2012

<table>
<thead>
<tr>
<th>Time from onset to treatment</th>
<th>Absolute growth</th>
<th>Favors Favors</th>
<th>Reduction in Volume</th>
<th>$P$ for</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intensive</td>
<td>Guideline</td>
<td>intensive</td>
<td>guideline</td>
</tr>
<tr>
<td>&lt;2.9h</td>
<td>-4.4 ml</td>
<td>2.1 ml</td>
<td>6.5 ml</td>
<td>0.1</td>
</tr>
<tr>
<td>2.9-3.6h</td>
<td>0.1 ml</td>
<td>3.4 ml</td>
<td>3.3 ml</td>
<td></td>
</tr>
<tr>
<td>3.7-4.8h</td>
<td>-1.1 ml</td>
<td>-0.2 ml</td>
<td>0.9 ml</td>
<td></td>
</tr>
<tr>
<td>≥4.9h</td>
<td>-0.2 ml</td>
<td>0.4 ml</td>
<td>0.6 ml</td>
<td></td>
</tr>
</tbody>
</table>

Reduction in hematoma growth over 72h (ml)
FAST-BP Pilot Trial
--Sanossian et al

- Phase 2a dose escalation trial
- Prehospital stroke patients with SBP>180
  - Symptom onset <2 hours
- GTN vs. placebo
  - 0.2 mg/hr patch
  - 0.4 mg/hr patch
  - 0.4 mg sublingual spray + 0.4mg/hr patch
- Endpoints
  - Decrease in SBP by ED arrival (primary)
  - Decrease in ICH expansion among ICH patients
  - More rapid DTN TPA time in ischemic stroke TPA patients
“The Ischemic Cascade”

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--Heiss et al, Stroke 1999
Classification of Neuroprotective Agents

- Modulators of Excitatory Amino Acids
- Modulators of Calcium Influx
- Metabolic Activators
- Anti-edema Agents
- Inhibitors of Leukocyte Adhesion
- Free Radical Scavengers and Anti-Oxidants
- Promotors of Membrane Repair
- Unknown or Other Mechanism(s)
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
Six Design Defects of Past Neuroprotective Trials

• Dose too low
  » Side effects
• Enroll patients unlikely to respond to drug action
  » White matter strokes for EAA blockade agents
• Enroll uninformative patients
  » Too mild at entry – fare well with placebo
  » Too severe at entry – fare poorly with active
• Sample sizes too small
• Outcome measures insensitive to modest but important benefits
• Late time of treatment start
Possible Therapeutic Effects of Magnesium in Stroke

**Vascular**
- Increased Cardiac Output
- Increased Regional CBF
- NMDA Ion Channel Blockade
- \( \text{Ca}^{2+} \) Channel Blockade
- Enhanced ATP Recovery

**Neuronal**
- \( \text{Mg}^{2+} \)
Prehospital Stroke Neuroprotective Trials: Distinctive Methodologic Aspects

• Diagnosing stroke in the field
  » Prehospital stroke identification instrument
• Rating stroke pretreatment severity
  » Prehospital stroke severity scale
• Eliciting consent
  » Strategy for obtaining field consent
• Characterizing early, field response to therapy
  » Prehospital course monitoring instrument
Characterizing Stroke Severity in the Field

- Glasgow Coma Scale
  » Level of consciousness, not focal stroke
- NIH Stroke Scale – Smith
  » Lengthy
- Shortened NIH Stroke Scale – Tirschwell
  » 5 items, not yet validated
- Los Angeles Motor Scale (LAMS)
Construction of the Los Angeles Motor Scale

- Point values assigned to each LAPSS exam element
  - Facial weakness (0, 1)
  - Arm strength (0, 1, 2)
  - Grip (0, 1, 2)
- Total score 0-5
Enrollment Times in 6 Recent Neuroprotective Trials (n=5345)
--Fergueson, Kidwell, Starkman, Saver, JSCVD 2004

More than 3 hrs

92.3%

UCLA Stroke Center
Enrollment Times in 6 Recent Neuroprotective Trials (n=5345)
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UCLA Stroke Center

More than 3 hrs: 92.3%
2-3 hrs: 6.3%
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<tr>
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<tr>
<td>--Ferguson, Kidwell, Starkman, Saver, JSCVD 2004</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2 hrs</td>
<td>1.2%</td>
</tr>
<tr>
<td>2-3 hrs</td>
<td>6.3%</td>
</tr>
<tr>
<td>More than 3 hrs</td>
<td>92.3%</td>
</tr>
</tbody>
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UCLA Stroke Center
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--Fergueson, Kidwell, Starkman, Saver, JSCVD 2004

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- 1-2 hrs: 1.2%
- 0-1 hrs: 0.2%

UCLA Stroke Center
Possible Therapeutic Effects of Magnesium in Stroke

**Vascular**
- Increased Cardiac Output
- Increased Regional CBF
- NMDA Ion Channel Blockade
- Ca$^{2+}$ Channel Blockade
- Enhanced ATP Recovery

**Neuronal**
- Mg$^{2+}$
- Enhanced ATP Recovery
Trends Toward Benefit of Early Magnesium in Human Brain Ischemia

- Neuropsychologic deficits after carotid endarterectomy
  » Columbia CEA Trial
- Neuropsychologic deficits after CABG
  » Cleveland Clinic Trial
- Global brain ischemia after cardiac arrest
  » Brain-CPR Trial
- Cerebral palsy in preterm infants
  » ACTOMgS04 Trial
- Focal brain ischemia
  » IMAGES Trial <3h subgroup
Prehospital Stroke Neuroprotective Trials: Distinctive Methodologic Aspects

- Diagnosing stroke in the field
  » LAPSS
- Rating stroke pretreatment severity
  » LAMS
- Eliciting consent
  » Field cellphone to MD simulating
- Randomization system
  » Pre-encounter randomization
Characterizing Stroke Severity in the Field

- **Glasgow Coma Scale**
  » Level of consciousness, not focal stroke
- **NIH Stroke Scale – Smith**
  » Lengthy
- **Shortened NIH Stroke Scale – Tirschwell**
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  » Facial weakness (0,1)
  » Arm strength (0,1,2)
  » Grip (0,1, 2)
• Total score 0-5
Entry LAMS vs Entry NIHSS

202 acute patients, $r = .82$, $p < .0001$
LAMS vs NIHSS and sNIHSS at Entry: Correlations with 3 Month Outcome Measures

Supported by NIH-NINDS
Chain Cell Forwarding System

Direct Call

First On-Call Investigator

Call Forwarding (30 Seconds)

Second On-Call Investigator

Call Forwarding (30 Seconds)

Third On-Call Investigator

Call Forward to First Investigator (30 Seconds)

Voice-Over-Internet Phone (VOIP) System

Direct Call to VOIP System to English Line (Blue) and Spanish Line (Red)

Spanish-Line First On-Call Investigator

Spanish-Line Second On-Call Investigator

Spanish-Line Third On-Call Investigator

English-Line First On-Call Investigator

English-Line Second On-Call Investigator

English-Line Third On-Call Investigator
Improved Prehospital Communication and Data Transfer Via 4G Wireless
Pre-Encounter Randomization in the NIH FAST-MAG Trial

- KISS principle in prehospital research
- Each ambulance carries one “prerandomized” drug kit
- Restock within 24 hours
- Kit includes in hospital maintenance bag
<table>
<thead>
<tr>
<th></th>
<th>Time (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAST-MAG (n=20)</td>
<td>23 min (±12)</td>
</tr>
<tr>
<td>Prior Trials (n=26)</td>
<td>141 min (±70)</td>
</tr>
</tbody>
</table>

\[ p < 0.0001 \]

*Time Savings: 1 hr 58 min*
The Field Administration of Stroke Therapy – Magnesium (FAST-MAG) Phase III Trial
Field Administration of Stroke Treatment – Magnesium (FAST-MAG) Trial

- Placebo-controlled, double-blind, randomized
- Multicenter, single region
  - 59 hospitals, Los Angeles and Orange Counties
- 4 gm Mg field, 16 gm Mg maintenance x 24h
- 1700 patients, 1st patient Jan 2005
- Primary endpoint: Rankin Scale shift
FAST-MAG Trial Setting and Participating Sites

- Los Angeles and Orange Counties
- Ethnically diverse population 13.3 million
- 59 receiving hospitals
- 353 rescue ambulances
- 3300 paramedics
- > 650 emergency physicians
- > 150 neurologists, neurosurgeons
Trial Status 10/16/12

1660 patients enrolled

98%
Trial Status 10/10/12

40 patients to go!
### Patient Characteristics

(n=1470)

<table>
<thead>
<tr>
<th>Age</th>
<th>69 (range 39-95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>42%</td>
</tr>
<tr>
<td>Index Event Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Cerebral ischemia</td>
<td>71.9%</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td>24.4%</td>
</tr>
<tr>
<td>Stroke Mimic</td>
<td>3.7%</td>
</tr>
<tr>
<td>Stroke Severity</td>
<td></td>
</tr>
<tr>
<td>LAMS (prehospital)</td>
<td>4.0 (range 1-5)</td>
</tr>
<tr>
<td>NIHSS (hospital arrival, after Rx start)</td>
<td>11.4 (range 0-40)</td>
</tr>
</tbody>
</table>
Key Treatment Intervals  
(n=1470)

- Stroke onset to study drug (median): 46 mins
- Paramedic arrival on scene to drug (mean): 25 mins
- Paramedic arrival on scene to ED (mean): 35 mins
- Treated within 1 hour of onset: 73%
- Treated 1-2 hr after onset: 24%

NIH-NINDS
## Concomitant IV TPA Therapy

(n=1470)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV TPA (among all cerebral ischemia pts)</td>
<td>34%</td>
</tr>
<tr>
<td>IV TPA (among ischemic stroke pts)</td>
<td>40%</td>
</tr>
</tbody>
</table>
Enrollment Times in 6 Recent Neuroprotective Trials (n=5345) -- Ferguson, Kidwell, Starkman, Saver, JSCVD 2004

- More than 3 hrs: 92.3%
- 2-3 hrs: 6.3%
- 1-2 hrs: 1.2%
- 0-1 hrs: 0.2%

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Enrollments in the Golden Hour
6 Recent Neuroprotective Trials

UCLA Stroke Center
Enrollments in the Golden Hour
6 Recent Neuroprotective Trials
vs FAST-MAG
IMAGES Trial Time to Treatment

0 0.7 2.6 8.2 13 12.2 11.3 11.8 10.3 7.6 8.8 13.5
FAST-MAG vs IMAGES
Time to Treatment

<table>
<thead>
<tr>
<th>Time (in minutes)</th>
<th>FAST-MAG</th>
<th>IMAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>8.2</td>
<td></td>
</tr>
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<td>5</td>
<td>13</td>
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<td>6</td>
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<td>9</td>
<td>10.3</td>
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<td>10</td>
<td>7.6</td>
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<td>11</td>
<td>8.8</td>
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<tr>
<td>12+</td>
<td>13.5</td>
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</tbody>
</table>
NINDS-TPA Study Time to Treatment

- 0-1: 75
- 1-2: 24
- >2: 1

NINDS-TPA Study
- 0-1: 0.3
- 1-2: 55
- >2: 1

FAST-MAG
- 0-1: 44.8
FAST-MAG Innovations

• First “golden hour” (<1 hr) stroke treatment trial
• First acute (<3 hr) neuroprotective stroke treatment trial
• First trial of neuroprotective drugs before recanalization therapies
• First prehospital stroke RCT
• First prehospital RCT for any condition employing physician-elicited informed consent
Impact

• Reinvigorate neuroprotective trials by delivering therapy to humans in the time windows in which they work in animal models
• Treatment could reach 20-50% of the 600,000 ischemic stroke patients in US each year
• Improve the outcome of up to 100,000 Americans per year
Acute Ischemic Stroke Treatment 1.0: IV TPA and Moderately Effective Endovascular Therapy

1. Symptoms
2. Call 911
3. Emergency Medical Services (EMS)
4. Primary Stroke Center
5. Imaging
6. Intravenous Lytic Therapy (IV Lytic)
Acute Ischemic Stroke Treatment 2.0: Fast and Furious