Overview of new acute stroke trials

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Some ischemic stroke patients benefit from intervention / thrombectomy
Recanalization futile in others
Improvements in procedural success with use of stentrievers

- SOLITAIRE™ FR (Covidien, Irvine, CA)
- TREVO™ (Concentric Medical, Mountain View, CA)

Clinical trials underway to ‘prove’ treatment works
Interventional Trials 2013

- IMS3 (Broderick et al)
- MR-RESCUE (Kidwell et al)
- SYNTHESIS (Ciccone et al)

- Neutral results
- Changed practice
- Impacted reimbursement of treatment
Criticisms of these trials

- End point of incomplete perfusion
- Delay in CT to groin puncture/recanalization
- Enrollment bias
- Long enrollment process
- Old technology
Interventional trials 2014-2015

- MR CLEAN (Berkhemer et al)
- ESCAPE (Goyal et al)
- EXTEND-IA (Campbell et al)
- SWIFT-PRIME (Saver et al)
- REVASCAT (Jovin et al)
Commonalities to 2014-2015 trials

- Documentation of vessel occlusion required
- Specified time to treatment
  - Median stroke onset to treatment ~4 hours
- Recanalization endpoint of TICI 2b or 3
- Rapid enrollment of patients
- mRS (modified Rankin Scale) score as primary outcome
- Homogeneity of clinical and radiographic benefit
  - Number needed to treat in single digits
MR CLEAN – Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands

- All patients from the Netherlands
- 6 hour window; any type of mechanical/chemical treatment
- Selection based on vessel imaging
  - CTA/MRA/DSA based selection
  - ICA, ACA, M1, or M2
- Primary outcome: modified Rankin Scale (mRS) score at 90 days
  - Good outcome as mRS of 0-3
MR CLEAN

- 500 patients
- NIHSS 17 (18 controls)
  - 87% treated with IV tPA (91% controls)
- 97% retrievable stents
- Median ASPECTS 9
- TICI 2b/3 59% (24% TICI 3)
- Stroke onset to groin puncture 260 min
- Infarct volume at 7 days 49 mL (79 mL in controls)
- Mortality at 30 days: 18.9% vs 18.4% (NS)
- Symptomatic ICH: 7.7% vs 6.4% (NS)

- Number needed to treat for mRS ≤2: 8
MR CLEAN

Control (N=267)

Intervention (N=233)

mRS Score □ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6

Berkhemer et al, NEJM, 2014
ESCAPE – (Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times)

- Primarily based out of Canada
- 12 hour window for enrollment
- CT/CTA (multiphase) based selection
  - ASPECTS score 6 or greater
  - Proximal (ICA and/or M1) occlusion
  - Moderate to good collaterals on CTA
- CT to groin: 60 min; CT to recan: 90 min
- Primary outcome: mRS score at 90 days
- Stopped at (unplanned) interim analysis
ESCAPE

- 311 patients (stopped early due to efficacy)
- NIHSS prior to treatment: 16 (17 in controls)
- 75% received IV - tPA
- 86% retrievable stents
- Median ASPECTS 9
- 72% TICI 2b/3 at end of procedure
- Stroke onset to reperfusion 241 minutes
- Mortality 10% vs 19% (p=0.04)
- Symptomatic ICH 3.6% vs 2.7% (NS)

- Number needed to treat for mRS score ≤2: 4
  - 3 for shift in mRS
ESCAPE

Control Overall (N=147)
Intervention Overall (N=164)
Control tPA (N=116)
Intervention tPA (N=119)
Control no tPA (N=31)
Intervention no tPA (N=45)

mRS Score □ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6

Hill et al, NEJM, 2015
EXTEND- IA: Extending the Time for Thrombolysis in Emergency Neurological Deficits – Intra-Arterial

- Primarily out of Australia
- 6 hour window, tPA alone vs tPA plus IA (Solitaire)
- MRI based selection
  - RAPID software
  - ICA, M1 or M2 occlusion
  - Mismatch with core <70 mL
- Primary outcomes: MRI at 24 hours and early clinical improvement (3 day NIHSS)
EXTEND-IA

- 70 patients total (stopped early due to efficacy)
- NIHSS prior to treatment 17 (13 controls)
- Baseline ischemic core 12 mL; penumbra 106 mL (core 18 mL in controls)
  - 24 hour ischemic core 18 mL (49 mL in controls)
- CT to groin puncture 93 min
- Onset to completion/reperfusion 248 min
- 86% TICI 2b or 3 (48% TICI 3)
- MRI evidence of reperfusion 100% vs 37% (p<0.001)
- Early improvement 80% vs 37% (p<0.001)
- Mortality 9% vs 20% (NS)
- Symptomatic ICH 0% vs 6% (NS)

- Number need to treat for mRS score ≤2: 4
  - 3 for shift in mRS
EXTEND- IA

Campbell et al, NEJM, 2015
SWIFT-PRIME: SOLITAIRE™ FR With the Intention For Thrombectomy as PRIMary Endovascular Treatment for Acute Ischemic Stroke

- US and European sites
- 6 hour window (to groin puncture); IV tPA and SOLITAIRE vs IV tPA alone
- CTA or MRA confirmation of ICA or M1 occlusion (no cervical carotid occlusion)
- ASPECT score ≥6, core lesion ≤50 mL, target mismatch ratio >1.8

- Primary outcome: mRS at 3 months
  - mRS 0-2 considered good outcome
SWIFT PRIME

- 195 patients (stopped at interim analysis)
- NIHSS prior to treatment 17
- 88% TICI 2b/3 (69% TICI 3)
- CT to groin puncture 57 min
- Onset to stent deployment 252 min
- Mortality at 90 days 9% vs 12% (NS)
- Symptomatic hemorrhage 0% vs 3% (NS)
- Number needed to treat for mRS≤2: 4
  - 2.6 for shift in mRS
SWIFT PRIME

IV tPA alone (N=97)

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5 &amp; 6</th>
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<tbody>
<tr>
<td>N=97</td>
<td>9</td>
<td>11</td>
<td>16</td>
<td>17</td>
<td>22</td>
<td>26</td>
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</table>

IV plus IA (N=98)

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5 &amp; 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=98</td>
<td>17</td>
<td>26</td>
<td>17</td>
<td>12</td>
<td>15</td>
<td>12</td>
</tr>
</tbody>
</table>

Saver et al, NEJM, 2015
REVASCAT: Randomized Trial of Revascularization with Solitaire FR Device vs Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within 8 Hours of Symptom Onset

- Patients from Catalonia, Spain
- 8 hour window to treatment; best medical therapy +/- Solitaire
- ICA, M1 or M2 occlusion
- ASPECT score ≥7 (CT) or ≥6 (MRI)
- Primary outcome: mRS at 3 months
**REVASCAT**

- 206 patients total; NIHSS prior to treatment 17
- ASPECTS score 7
- 66% TICI 2b or 3 (19% TICI 3)
- CT to groin puncture 77 min*
- Onset to revascularization 355 min
- 24 hour infarct volume 16mL vs 39 mL (p=0.02)
- Mortality at 90 days 18% vs 15% (NS)
- Symptomatic hemorrhage 5% vs 2% (NS)

- Number needed to treat for mRS ≤ 2: 7
REVASCAT

Control (N=103)

Thrombectomy (N=103)

Jovin et al, NEJM, 2015
# Summary

<table>
<thead>
<tr>
<th>Trial</th>
<th># of Patients</th>
<th>% tPA</th>
<th>ASPECTS (range)</th>
<th>TICI 2b/c</th>
<th>Onset to IA treatment</th>
<th>NNT mRS ≤2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR Clean</td>
<td>500/233</td>
<td>87</td>
<td>9 (0-10)</td>
<td>59%</td>
<td>260*</td>
<td>8</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>311/164</td>
<td>73</td>
<td>9 (6-10)</td>
<td>72%</td>
<td>185*/241‡</td>
<td>4</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>70/35</td>
<td>100</td>
<td>n/a</td>
<td>86%</td>
<td>210*/248‡</td>
<td>4</td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>196/98</td>
<td>100</td>
<td>9 (6-10)</td>
<td>88%</td>
<td>224*/252‡</td>
<td>4</td>
</tr>
<tr>
<td>REVASCAT</td>
<td>206/103</td>
<td>68</td>
<td>7 (6-10)</td>
<td>66%</td>
<td>269*/355‡</td>
<td>7</td>
</tr>
</tbody>
</table>

*: groin puncture  
†: stent deployment  
‡: recanalization/end of procedure
Summary

- Thrombectomy is efficacious in treating ischemic stroke patients with:
  - Proximal occlusion
  - Favorable imaging profile
  - Recent symptom onset