Recent Progress In Endovascular Intracranial Treatment Of Acute Ischemic Strokes: Dramatic Positive Results Of ESCAPE, SWIFT-PRIME, EXTEND – IA, REVASCAT And MR CLEAN Trials: Why Are These Trials Positive And When Should Patients Be Treated And Why

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Disclosure Statement of Financial Interest

- Grant/Research Support
- Consulting Fees/Honoraria
- Major Stock Shareholder/Equity
- Royalty Income
- Ownership/Founder
- Intellectual Property Rights
- Other Financial Benefit

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

- Toshiba, Medtronic, Microvention
- None
- None
- None
- None
- None

Options for Patients Experiencing an Ischemic Stroke

**Endovascular Clot Removal**
Mechanical disruption or removal of the clot using standard endovascular approaches

**Bridging Therapy**
Medication to bridge patients to endovascular clot removal

**IV tPA**
Gold-standard in ischemic stroke care. Drug is designed to break apart the clot.

**Medical Management**
Monitor vitals and provide secondary stroke prevention.

**Bridging**
Therapy - Non FDA-Approved Therapies

IV tPA, the OLD “Gold Standard”
- FDA Approved for the tx of AIS in 1996
- Only 8% of ischemic stroke patients are eligible
- Narrow time window
- Risk of cerebral and systemic hemorrhage
- Achieves early reperfusion in only 13-50% of large vessel occlusions
- >60% of patients dead or disabled at 3 months

Meta-analysis Shows a Strong Correlation Between Revascularization and Good Patient Outcomes

- 58.1% Good Outcome
- 26.4% In-Hospital Mortality
- 10.5% sICH
- 13.7% Mortality
- 24.8% Good Outcome
- 12.5% In-Hospital Mortality
- 0% sICH

 diferença é estatisticamente significativa entre os grupos de revascularização e não-revascularização. *P<0.05. The impact of revascularization on ischemic stroke outcome a meta-analysis. Stroke, 2012
Goal of Ischemic Stroke Treatment

35-40% of Ischemic Strokes are "Large Vessel" occlusions
- This subset of AIS comprises blockages in the:
  - Internal Carotid Artery (ICA)
  - Middle Cerebral Artery (MCA)
  - Vertebral / Basilar Artery
- Patient prognosis with these types of stroke is poor

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>53%¹</td>
</tr>
<tr>
<td>MCA</td>
<td>27%²</td>
</tr>
<tr>
<td>Basilar Artery</td>
<td>85-90%³</td>
</tr>
</tbody>
</table>

Previous Stroke Trials Failed to Show Benefit in Endovascular
- IMS 3, MR RESCUE, SYNTHESIS-Expansion

What did we learn?
- Imaging to confirm large vessel occlusion
- Imaging to exclude pts with a large infarct core
- Improve time to treatment
- Newest devices improve recanalization rates
- Endovascular approach is SAFE

NEW TRIALS
- MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT
- With minor variations, compared:
  - IV-tPA alone
  - IV-tPA + endovascular therapy

Reliable Revascularization

Endovascular Triage and Therapy Does Note Delay Treatment Initiation

<table>
<thead>
<tr>
<th>Study</th>
<th>TICI 2a or 3</th>
<th>TICI 2b</th>
<th>TICI 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR CLEAN</td>
<td>115/196 (58.7%)</td>
<td>68/196 (34.7%)</td>
<td>47/196 (24%)</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>21/29 (72%)</td>
<td>11/29 (38%)</td>
<td>14/29 (48%)</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>115/116 (98%)</td>
<td>data not available</td>
<td>data not available</td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>71/83 (86%)</td>
<td>16/83 (19.3%)</td>
<td>57/83 (68.7%)</td>
</tr>
<tr>
<td>REVASCAT</td>
<td>63/102 (61.7%)</td>
<td>46/102 (45.1%)</td>
<td>19/102 (18.6%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>From symptom onset to IV-ipa*</th>
<th>From symptom onset to groin puncture</th>
<th>From groin puncture to recanalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR CLEAN</td>
<td>87 (67-110)</td>
<td>87 (65-116)</td>
<td>260</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>145 (105-190)</td>
<td>210</td>
<td>93</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>120 (90-140)</td>
<td>185</td>
<td>96</td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>117 (86-155)</td>
<td>117 (86-155)</td>
<td>224</td>
</tr>
<tr>
<td>REVASCAT</td>
<td>117 (90-150)</td>
<td>105 (86-137.5)</td>
<td>260</td>
</tr>
</tbody>
</table>

* From symptom onset to IV-ipa: 66-100 min
Safe

Overwhelming Benefit for Intervention

- MR CLEAN
- ESCAPE
- EXTEND-IA
- SWIFT PRIME
- REVASCAT

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<table>
<thead>
<tr>
<th>Study</th>
<th>Symptomatic ICH</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV-PA Alone</td>
<td>IV-PA Alone</td>
</tr>
<tr>
<td>MR CLEAN</td>
<td>18 (17.7%)</td>
<td>17 (16.3%)</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>0 (0%)</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>6 (3.6%)</td>
<td>4 (2.7%)</td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>0 (0%)</td>
<td>3 (1.1%)</td>
</tr>
<tr>
<td>REVASCAT</td>
<td>5 (4.9%)</td>
<td>2 (1.8%)</td>
</tr>
</tbody>
</table>

Swift Prime: NEJM Conclusions

- In AIS patients with confirmed LVO treated with IV-PA + Clot Retrievers lessens post-stroke disability and increases the proportion of patients who are alive and independent 3 months after stroke
- For every two and a half patients treated, one more patient has a better disability outcome
- For every four patients treated, one more patient is independent at long term follow up

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AHA/ASA Guideline

New Recommendation

- Patients should receive endovascular therapy with a stent retriever
  
- If they meet all the following criteria (Class I; Level of Evidence A).
  
  (a) Pre-stroke mRS score 0 to 1
  
  (b) Acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset

New Recommendation

- (c) causative occlusion of the internal carotid artery or proximal MCA (M1),
- (d) age ≥18 years,
- (e) NIHSS score of ≥6,
- (f) CT shows small core infarct (ASPECTS of ≥6)
- (g) treatment can be initiated (groin puncture) within 6 hours of symptom onset
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