The Analysis of Revascularization in Ischemic Stroke With EmboTrap (ARISE II Trial)


On behalf of the ARISE II investigators
Disclosures

• Consultant for Neuravi, now Cerenovus
Background

• Newer generation mechanical thrombectomy devices significantly improved outcomes in acute ischemic stroke therapy.

• However limitation to current technology exists:

  • Failure to achieve successful reperfusion (mTICI≥2b) in ~ 1/3 of the patients (In the Seers and Hermes RCT pooled analysis; the reperfusion rate reported at 71%).

  • Limited rate of Final near complete or complete (TICI 2c-3) reperfusion, with reported rates of up to 50%

  • Furthermore, First Pass/Attempt near complete or complete reperfusion was reported at still low rates of up to 30% (self and core lab reported)


Background: EmboTrap Device

• EmboTrap Revascularization Device:
  ➢ Engineered on a foundation of extensive clot research
  ➢ Inner channel to allow for temporary bypass
  ➢ Outer cage for clot-device interaction
  ➢ Distal protection zone
ARISE II Team

Participating Sites:
- 19 Sites: 11 US sites, 8 European sites

Executive Committee
- Osama Zaidat, MD (Study PI)
- Tommy Andersson, MD (Study PI)
- Heinrich Mattle, MD
- Jeffrey Saver, MD
- Mairsil Claffey – Sponsor Representative

Steering Committee
- Hormozd Bozorgchami, MD
- Marc Ribo, MD
- Adnan Siddiqui, MD
- Ashutosh Jadhav, MD
- Ana Paula Narata, MD
- Albert Yoo, MD
- Rene Chapot, MD
- Jonathan Grossberg, MD

DSMB
- Steven Hetts, MD Chair
- Werner Hacke, MD
- Lotfi Hacein-Bey, MD
- Brijesh Mehta, MD
- Anthony Kim, MD
- Alex Abou-Chebl, MD
- Peter Shabe (Biostatistician)

CEC
- Steven Hetts, MD, Chair
- Lotfi Hacein-Bey, MD
- Anthony Kim, MD
- Alex Abou-Chebl, MD

Core Lab
- Albert Yoo, MD Core Lab Director
- Intrinsic Imaging LLC (Massachusetts)

Sponsor
- Neuravi, now Cerenovus
Study Objectives

Primary objectives:
• Assess the revascularization and safety outcomes of the EmboTrap device in acute ischemic stroke

Secondary objectives:
• Functional clinical outcomes at 90 days post treatment
Methods

- Study Design:
  - Open label, single arm, multi-center, prospective clinical study
  - Independent imaging core lab
  - Independent clinical event committee and DSMB
- Designed to secure 510(k) clearance of the EmboTrap® Revascularization Device
- Population: Anterior and Posterior Circulation LVO presenting with acute ischemic stroke
- Sample Size: Based on pre-specified performance goal from TREVO2, and SWIFT trials result. With an assumption of independently adjudicated revascularization success with EmboTrap is 68%; 176 patients would provide 90% power and 0.025 significance level.
- Final Sample Size 228, to allow for 30% Attrition rate
Method: ARISE II Study Endpoints

<table>
<thead>
<tr>
<th>Primary Efficacy Endpoint</th>
<th>• mTICI 2b-3 within 3 passes of the EmboTrap device without rescue <em>(inclusive of 2c rating) (core-lab adjudicated)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Safety Endpoint</td>
<td>• Composite of occurrence of symptomatic intra-cerebral hemorrhage <em>(sICH)</em> within 24 hours post-procedure, together with other serious adverse device events <em>(CEC adjudicated)</em></td>
</tr>
</tbody>
</table>
| Secondary Endpoints       | • modified Rankin Score *(mRS)* ≤2 at 90 days  
  • Procedure and time to treat  
  • Mortality rate (Procedure-related at 7d, all-cause at 90d)  
  • SADE (serious adverse device events)  
  • Neurological deterioration by ≥4 points on NIHSS at 24 hrs |
Method: Angiographic outcome measure

• The revascularization grading was performed using mTICI scale
• The independent core lab adjudicated the angiograms after:
  • Each Device Pass/Attempt providing independent adjudication of First Pass Effect
  • Three Passes (the primary study endpoint)
  • At the end of the procedure
• Use of a different device prior to 3 passes was considered failure
• Use of Aspiration Pump with any device pass was considered failure
RESULTS
ARISE II Enrollment Rate: 228 enrolled

- Total enrolled with LVO: 228
- Total treated with EmboTrap: 227
- Total treated in the US: 101
- Total treated in Europe: 126
Method: Study Flow Chart

- 5 lost to follow-up
- All patients had angiographic follow-up
## DEMOGRAPHIC

<table>
<thead>
<tr>
<th>Demographics</th>
<th>ARISE II Treated (N = 227)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years] Mean (SD)</td>
<td>68.0 (13)</td>
</tr>
<tr>
<td>Male [% (n)]</td>
<td>45.8% (104)</td>
</tr>
<tr>
<td>NIHSS</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>15.8 (5)</td>
</tr>
<tr>
<td>Median</td>
<td>16</td>
</tr>
<tr>
<td>Treated with IV-tPA [% ,n]</td>
<td>66.1% (150)</td>
</tr>
<tr>
<td>Pre Stroke Modified Rankin Score [% (n)]</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>78% (177)</td>
</tr>
<tr>
<td>1</td>
<td>21.6% (49)</td>
</tr>
<tr>
<td>2</td>
<td>0.4% (1)</td>
</tr>
</tbody>
</table>
## Co-Morbidities

<table>
<thead>
<tr>
<th>Medical History</th>
<th>Treated (N = 227)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>68.3% (155)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19.8% (45)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>39.6% (90)</td>
</tr>
<tr>
<td>Previous Stroke / TIA</td>
<td>18.9% (43)</td>
</tr>
<tr>
<td>Previous MI / CAD</td>
<td>19.8% (45)</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>43.2% (98)</td>
</tr>
<tr>
<td>Smoking</td>
<td>24.7% (56)</td>
</tr>
</tbody>
</table>
RESULTS: Workflow in Median with IQR

<table>
<thead>
<tr>
<th>Event</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset to revascularization</td>
<td>243 (183-303)</td>
</tr>
<tr>
<td>Onset to puncture</td>
<td>214 (155-266)</td>
</tr>
<tr>
<td>First hospital to enrolling hospital</td>
<td>129 (108-162)</td>
</tr>
<tr>
<td>Door to puncture</td>
<td>60 (36-93)</td>
</tr>
<tr>
<td>Door to imaging</td>
<td>15 (9-26)</td>
</tr>
<tr>
<td>Puncture to revascularization</td>
<td>45 (27-70)</td>
</tr>
<tr>
<td>Time to treat (first angiogram to revascularization)</td>
<td>24 (13-45)</td>
</tr>
</tbody>
</table>
### Clot Locations per Core Lab

<table>
<thead>
<tr>
<th>Location</th>
<th>Treated (N=227)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anterior Circulation [% (n)]</strong></td>
<td></td>
</tr>
<tr>
<td>• Internal carotid artery</td>
<td>96% (218)</td>
</tr>
<tr>
<td>• M1 middle cerebral artery</td>
<td>15.4% (35)</td>
</tr>
<tr>
<td>• M2 middle cerebral artery</td>
<td>55.5% (126)</td>
</tr>
<tr>
<td><strong>Posterior Circulation [% (n)]</strong></td>
<td></td>
</tr>
<tr>
<td>• Basilar Artery</td>
<td>4% (9)</td>
</tr>
<tr>
<td>• Vertebral Artery</td>
<td>0% (0)</td>
</tr>
</tbody>
</table>
Procedural Results

<table>
<thead>
<tr>
<th>Procedural Information [% (n)]</th>
<th>Treated (N = 227)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon Guide Catheter Use</td>
<td>73.6% (167)</td>
</tr>
<tr>
<td>Intermediate Catheter Use</td>
<td>41% (93)</td>
</tr>
</tbody>
</table>

One procedure may have more than one technique
ARISE II PRIMARY AND SECONDARY ENDPOINTS RESULTS
### ARISE II Revascularization Outcome

#### 80% mTICI 2b-3

<table>
<thead>
<tr>
<th>mTICI</th>
<th>Percentage</th>
<th><strong>Treated (n=227)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>mTICI 3</td>
<td>43.6% (99/227)</td>
<td></td>
</tr>
<tr>
<td>mTICI 2c</td>
<td>21.1% (48/227)</td>
<td></td>
</tr>
<tr>
<td>mTICI 2b</td>
<td>15.4% (35/227)</td>
<td></td>
</tr>
<tr>
<td>mTICI 2a</td>
<td>5.3% (12/227)</td>
<td></td>
</tr>
<tr>
<td>mTICI 1</td>
<td>2.6% (6/227)</td>
<td></td>
</tr>
<tr>
<td>mTICI 0</td>
<td>10.6% (24/227)</td>
<td></td>
</tr>
</tbody>
</table>

*The numerator does not sum to 227 as 3 patients had rescue therapy prior to 3rd pass and their angiographic results were not included.*
ARISE II Revascularization Outcome

Final
- mTICI 2b-3: 93%
- 52% successful
- 24% incomplete
- 17% failed
- 3% unsuccessful

Within 3 Passes of EmboTrap
- mTICI 2b-3: 80%
- 44% successful
- 21% incomplete
- 15% failed
- 5% unsuccessful

First Pass Effect
- mTICI 2b-3: 51.5%
- 30% successful
- 10% incomplete
- 11% failed
- 14% unsuccessful

N=227, angiographic outcomes for 3 cases where rescue therapy was used prior to third pass were not included in w/in 3 passes of EmboTrap revascularization.
ARISE II Revascularization Rate Per Pass

<table>
<thead>
<tr>
<th>First Pass Reperfusion with EmboTrap</th>
<th>Treated (n=227)</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-Pass mTICI 2c-3</td>
<td>40.1% (91/227)</td>
</tr>
<tr>
<td>One-Pass mTICI 2b-3</td>
<td>51.5% (117/227)</td>
</tr>
</tbody>
</table>

Reperfusion by Pass

- 52% mTICI 0
- 69% mTICI 1
- mTICI 2a
- mTICI 2b
- mTICI 2c
- mTICI 3
ARISE II Clinical Endpoints

mRS 0-2: 67.3%

mRS 0-1: 51.6%

mRS in Treated cohort includes all those treated with rescue therapy but excludes cases where the patient withdrew consent or was lost to follow up with undefined/unknown scores.
### ARISE II Safety Results

<table>
<thead>
<tr>
<th>Safety Event</th>
<th>Treated (n=227)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Safety Endpoint</strong></td>
<td></td>
</tr>
<tr>
<td>sICH within 24 hours in combination with other SADE</td>
<td>5.3% (95%CI: 3-9%)</td>
</tr>
<tr>
<td>Neurological deterioration by 4 NIHSS points or more at 24hr</td>
<td>4.5% (95%CI: 2-9%)*</td>
</tr>
<tr>
<td>Procedure-related mortality at day 7</td>
<td>0.0% (95%CI: 0-2%)</td>
</tr>
<tr>
<td>All-cause mortality at 90 days</td>
<td>9.0% (95%CI: 6-14%)</td>
</tr>
<tr>
<td>Embolization into new territory</td>
<td>6.6% (95%CI: 4-11%)</td>
</tr>
</tbody>
</table>

*Absence or presence of neurological deterioration was only documented in 178 patients*
ARISE II: Use of other devices (rescue)

<table>
<thead>
<tr>
<th>Rescue Therapy</th>
<th>Treated (n=227)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with rescue therapy</td>
<td>19.4% (44/227)</td>
</tr>
<tr>
<td>Type of rescue therapy used:</td>
<td></td>
</tr>
<tr>
<td>Mechanical thrombectomy device</td>
<td>16.3% (37/227)</td>
</tr>
<tr>
<td>Mechanical pump aspiration</td>
<td>3.1% (7/227)</td>
</tr>
<tr>
<td>IA tPA</td>
<td>0.9% (2/227)</td>
</tr>
<tr>
<td>Intracranial stenting</td>
<td>0.9% (2/227)</td>
</tr>
<tr>
<td>Other</td>
<td>3.5% (8/227)</td>
</tr>
</tbody>
</table>
ARISE II PRIMARY RESULTS

DISCUSSION
Comparison to recent RCT’s Final Revasc Success Rate

mTICI 2b-3 Reperfusion

93%
Device Final Complete Revasc Rate vs RCT

mTICI 3 Reperfusion

52%
Comparison to recent RCT’s: mRS Results

Treated cohort results as reported, includes rescue
sICH RESULTS COMPARED TO RCT
MORTALITY RESULTS VS RECENT RCT

All-Cause Mortality at 90 days

- ARISE II
- SEER
- Hermes
- REVASCAT
- SWIFT PRIME
- MR Clean
- DAWN
- EXTEND IA
- ESCAPE
- THRACE
- ASTER (SR 1st)
- ASTER (Asp 1st)
Summary

- EmboTrap achieved high reperfusion rate in LVO patients:
  - 64.8% mTICI 2c-3 within 3 passes of the EmboTrap
  - **80.2% mTICI 2b-3 within 3 passes (Study Endpoint)**
  - 92.5% mTICI 2b-3 final procedural revascularization
- Promising one-pass success:
  - 51.5% mTICI 2b-3 successful first-pass reperfusion
  - 40.1% mTICI 2c-3 excellent first-pass reperfusion
- Treated patients had good outcomes
  - Functional independence in 67.3% (mRS 0-2)
  - Highly functional independence in 51.6% (mRS 0-1)
  - sICH rate of 5.4% and 90-day Mortality of 9%

Caution: Investigational Device. Limited by Federal Law to investigational use only.
“Uncertainty is DEFUSED, a new day DAWNs, and we ARISE to meet it with the scientific COMPASS” Jeff Saver, MD
Thanks to Enrolling Sites PIs, Sub-PIs, CRCs, Patients and Their Families

United States
- OHSU, OR
- UPMC, PA
- Emory, GA
- Mercy St. Vincent Medical Center, OH
- Kaleida Health, Buffalo, NY
- Riverside Radiology, OH
- Banner Desert Med. Center, AZ
- Tennessee Interventional / Erlanger, TN
- Good Samaritan Hospital / Regional Med Ctr, CA
- Mount Sinai, NY
- UCLA, CA

Europe
- Hospital Vall d’Hebron – Spain
- Alfred Krupp Krankenhaus – Germany
- CHRU de Tours – France
- AZ Groeninge – Belgium
- UKSH Kiel – Germany
- Beaumont Hospital – Ireland
- Universitätsklinikum Freiburg – Germany
- Inselspital, Bern - Switzerland
- UCLA Stroke Network
- Inselspital, Bern
- Mount Sinai
- Good Samaritan Hospital / Regional Med Ctr
- University of Buffalo/Kaleida
- Beaumont Hospital
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Total