WOVEN TRIAL
Wingspan One-Year Vascular Events and Neurologic Outcomes

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**Conflict of Interest Disclosure**

**Industry Sponsored Research**
WEAVE trial (NCT02034058) Principal Investigator

**Consulting / Device Proctoring**
Stryker Neurovascular – Consultant and device proctor

**N.I.H. Sponsored Research**
SAMMPRIS trial – (R01 NS036643) Initial N.I.H. study steering committee, Institutional PI
N.I.H. Wingspan Registry – (R01 NS051688) Steering committee and Institutional PI

The WOVEN Trial was not funded by industry
Registered at ClinicalTrials.gov NCT04221984
Background

Industry Funded (Stryker) Post Market Surveillance Trial
- FDA mandated trial evaluating peri-procedural stroke and death rate of Wingspan Stent System when used on-label
- On-label use only in 152 patients with 70% or greater stenosis from intracranial atherosclerosis, with two strokes, failed medical therapy, treated greater than 7 days post-stroke
- Peri-procedural event rate 2.6%
- ClinicalTrials.gov [NCT02034058](https://clinicaltrials.gov/ct2/show/NCT02034058)
- Stroke 2019 Apr;50(4):889-894. doi: 10.1161/STROKEAHA.118.023996

Physician initiated, not funded by industry
- Delayed stroke and death rate of patients treated on-label in the WEAVE Trial at one-year follow up
- 15 participating centers nationally
- Clinical and imaging follow up of 129 patients
- ClinicalTrials.gov [NCT04221984](https://clinicaltrials.gov/ct2/show/NCT04221984)
Intra-Cranial Atherosclerotic Disease (ICAD) represents a significant subset of stroke

- 8-10% of strokes in the United States are due to ICAD (approximately 50,000-70,000 symptomatic ICAD cases/year in the U.S.)
  - Sacco RL, et al., Stroke 26:14-20, 1995
- 46% of patients with strokes had ICAD in the CICAS study in China
Patient Presentation: Variable for ICAD, similar to AIS and LVO

<table>
<thead>
<tr>
<th></th>
<th>Hemodynamic compromise</th>
<th>Embolic</th>
<th>Perforator stroke alone</th>
<th>In-situ thrombosis with LVO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenting</td>
<td>++++</td>
<td>++</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Medical therapy</td>
<td>+</td>
<td>+++</td>
<td>++++</td>
<td>+/-</td>
</tr>
</tbody>
</table>

These patients have different risks and benefits for stenting and medical therapy alone.
# U.S. Prospective ICAD Wingspan Stent Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Publication</th>
<th>Number of Patients</th>
<th>On Label Stenting</th>
<th>Peri-procedural Complications</th>
<th>Time to Stent from Stroke/TIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wingspan HDE</td>
<td>Stroke 2007</td>
<td>44</td>
<td>93%</td>
<td>4.5%</td>
<td>22 days</td>
</tr>
<tr>
<td>NIH Registry</td>
<td>Neurology 2008</td>
<td>128</td>
<td>61%</td>
<td>6.2%</td>
<td>10 days</td>
</tr>
<tr>
<td>U.S. Wingspan Registry</td>
<td>Stroke 2007</td>
<td>78</td>
<td>58%</td>
<td>6.1%</td>
<td>No data</td>
</tr>
<tr>
<td>SAMMPRIS</td>
<td>NEJM 2011</td>
<td>208</td>
<td>8.2%</td>
<td>14.7%</td>
<td>7 days</td>
</tr>
<tr>
<td>WEAVE Trial</td>
<td>Stroke 2019</td>
<td>152</td>
<td>100%</td>
<td>2.6%</td>
<td>22 days</td>
</tr>
</tbody>
</table>
Outcomes Related to Time to Stenting: Meta-analysis

- **5** Yu SC, *JNIS* April 2014
- **4** Jiang WJ, *Stroke* July 2011
- **3** NIH. Wingspan Registry, *Neurology* 2008
- **2** SAMMPRIS Trial, *NEJM* 2011
- **1** WEAVE Trial, *Stroke* April 2019

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**Table:**

<table>
<thead>
<tr>
<th>Days to Stenting Post Event</th>
<th>Peri-procedural Complication Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7d WEAVE Registry</td>
<td>30</td>
</tr>
<tr>
<td>8-14d WEAVE</td>
<td>20</td>
</tr>
<tr>
<td>&gt;10d NIH Registry</td>
<td>10</td>
</tr>
<tr>
<td>&gt;15d WEAVE</td>
<td>0</td>
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</tbody>
</table>
What Factors May Lead to Poor Outcomes in Early Stenting?

Increased thrombogenicity and inflammatory processes with acutely ruptured atherosclerotic plaque

“Hot plaque” – Recently ruptured plaque is more thrombogenic, so adding a foreign body (stent) increases the risk for thrombo-embolic complications after early stenting

Bentzon JF et al,. Mechanisms of plaque formation and rupture

Risk of Stroke or Death Is Associated With the Timing of Carotid Artery Stenting for Symptomatic Carotid Stenosis: A Secondary Data Analysis of the German Statutory Quality Assurance Database

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Background—Subgroup analyses from randomized trials indicate that the time interval between the neurologic index event and carotid artery stenting is associated with periprocedural stroke and death rates in patients with symptomatic carotid stenosis. The aim of this article is to analyze whether this observation holds true under routine conditions in Germany.

Methods and Results—Secondary data analysis was done on 4717 elective carotid artery stenting procedures that were performed for symptomatic carotid stenosis. The patient cohort was divided into 4 groups according to the time interval between the index event and intervention (group I 0-2, II 3-7, III 8-14, and IV 15-180 days). Primary outcome was any in-hospital stroke or death. For risk-adjusted analyses, a multilevel multivariable regression model was used. The in-hospital stroke or death rate was 3.7% in total and 6.0%, 4.4%, 2.4%, and 3.0% in groups I, II, III, and IV, respectively. Adjusted analysis showed a decreased risk for any stroke or death in group III, a decreased risk for any major stroke or death in groups III and IV, and a decreased risk for any death in groups II and III compared to the reference group I.

Conclusions—A short time interval between the neurologic index event and carotid artery stenting of up to 7 days is associated with an increased risk for stroke or death under routine conditions in Germany. Although results cannot prove causal relationships, carotid artery stenting may be accompanied by an increased risk of stroke or death during the early period after the index event. (J Am Heart Assoc. 2018;7:e007983. DOI: 10.1161/JAHA.117.007983.)
- SAMMPRIS stenting poor results when used off-label
- Peri-procedural event rate must be <5% to be beneficial
Clinical Outcomes at one year
- Stroke in vascular territory of stented artery
- Neurologic Death

Delayed Imaging Outcomes
- Assessment of re-stenosis incidence and degree
- Symptomatic or asymptomatic stenosis
- Management of re-stenosis, retreatment
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- 15 of the original 24 WEAVE sites participated in WOVEN
- All 15 sites obtained study IRB approval and signed data usage agreements (DUAs)
- 3 sites still pending approval
- 129 patients of the original 152 WEAVE patients had one year follow up (85%)
- Chart and image review by research study group
Re-stenosis rates
• 107 of 129 patients (83%) with delayed imaging follow up
• Type of imaging
  • 62 Catheter angiography
  • 21 CTA
  • 19 MRA
  • 5 TCD
• 18 Patients (16.8%) with re-stenosis 70% or greater
• Mean time to re-stenosis dx – 5 months (range 1-11)
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Re-stenosis management

- 7 patients symptomatic
  - 3 patients managed medically
  - 3 patients with repeat angioplasty and stent
  - 1 patient with angioplasty alone
- 11 patients asymptomatic
  - 7 patients managed medically
  - 2 patients with repeat angioplasty and stent
  - 2 patient with angioplasty alone
WOVEN Trial Primary Endpoints beyond 30 days

Stroke in vascular territory of stent 7 pts
- Minor stroke (change ≤ 3 NIHSS points) 6 pts
- Major stroke (change > 3 NIHSS points) 1 pt
Non-traumatic cerebral hemorrhage 0 pts
Neurologic death 0 pts
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<table>
<thead>
<tr>
<th>Group</th>
<th># at Risk</th>
<th>Months after Randomization</th>
</tr>
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<tbody>
<tr>
<td>Medical Group</td>
<td>227</td>
<td>227</td>
</tr>
<tr>
<td></td>
<td>196</td>
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<td>92</td>
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<tr>
<td>PTAS Group</td>
<td>224</td>
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<td>98</td>
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<td></td>
<td>83</td>
<td>83</td>
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</tbody>
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- WASID 23%
- SAMMPRIS Stent 20%
- SAMMPRIS AMM 12.2%
- WOVEN 8.5%
Even with the poor trial conditions in SAMMPRIS, stenting gave long term protection from severe stroke

In SAMMPRIS, the percentage of patients with disabling or fatal strokes beyond 30 days was nearly 3 times higher in the medical therapy group, compared to the stenting group:

**STENTING GROUP: 2.2% rate**

**MEDICAL THERAPY: 6.2% rate**
### WOVEN Trial

**Wingspan One-Year Vascular Events and Neurologic Outcomes**

#### Long term event rate

<table>
<thead>
<tr>
<th></th>
<th>30 day Event rate</th>
<th>1 year Event rate</th>
<th>1 -12 month stroke rate</th>
<th>1-12 month severe stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAMMPRIS AMM</td>
<td>5.8 %</td>
<td>12.2 %</td>
<td>6.4 %</td>
<td>6.2 %</td>
</tr>
<tr>
<td>SAMMPRIS Stent arm</td>
<td>14.7 %</td>
<td>20.0 %</td>
<td>5.3 %</td>
<td>2.2 %</td>
</tr>
<tr>
<td>WOVEN Stent arm</td>
<td>2.6 %</td>
<td>8.5 %</td>
<td>5.9 %</td>
<td>0.8 %</td>
</tr>
</tbody>
</table>
Conclusions

The WOVEN Trial demonstrated an 8.5% one-year stroke and death rate in 129 patients stented on-label with the Wingspan stent, inclusive of the 4 patients who had peri-procedural events.

The re-stenosis rate was 16.8% in this cohort, and 7/18 of these patients (38.9%) were symptomatic. This was the primary cause of delayed stroke within the first year post-stenting.

The WOVEN 1-12 month event rate was similar to the stenting arm of SAMMPRIS. However, since the peri-procedural complication rate was very low (2.6%), the WOVEN study total 1-year stroke and death rate (8.5%) trended lower than aggressive medical therapy alone in SAMMPRIS at 1-year (12.2%).

This data strongly supports further randomized clinical trials for ICAD between stenting and medical therapy for the high-risk patients (with hemodynamic compromise) treated in an on-label fashion.
Acknowledgements

Santa Barbara
Wellstar Health
Central Baptist
Abington Memorial
Cleveland Clinic
Multicare Medical
Tennessee Intevent
UC Irvine
Dr. Alois Zauner
Dr. Rishi Gupta
Dr. Curtis Given
Dr. Larami Mackenzie
Dr. Gabor Toth
Dr. Brian Kott
Dr. Blaise Baxter
Dr. Wengui Yu
SSM DePaul
U. Kentucky
Cedars Sinai
Valley Baptist
Mount Sinai
Columbia
Cadence Health
Dr. Amer Al Shekhlee
Dr. Justin Fraser
Dr. Michael Alexander
Dr. Ameer Hassan
Dr. John Chaloupka
Dr. Philip Meyers
Dr. Harish Shownkeen

Research Coordinators

Vicki Manoukian
Gabriella Diaz
Janey Barnhart
Ashley Depalmo
Jennifer Isaacs
Laurie Preston
Erin Ross
Linda Breathitt
Kathy Hansen
Michelle Raymond
Jacquie Johnson