ROADSTER 2 Trial:
Transcervical access with reversed flow for proximal protection during CAS:
What have we learned so far?

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Disclosure

Peter A. Schneider

I have the following potential conflicts of interest to report:

Scientific Advisory Board (non-paid): Cardinal, Abbott, Medtronic

Royalty (modest): Cook

Co-founder and Chief Medical Officer: Intact, Cagent

Enter patients into studies: NIH, Bard, Gore, Medtronic, BSI, Silk Road (no financial relationship).

VIVA Board member (nonprofit)
Best Results for CAS in a Randomized Trial
Transfemoral with Distal Filter Protection

Any periprocedural stroke or death or postprocedural ipsilateral stroke

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic patients</td>
<td>15 (2.5±0.6)</td>
<td>8 (1.4±0.5)</td>
</tr>
<tr>
<td>Symptomatic patients</td>
<td>40 (6.0±0.9)</td>
<td>21 (3.2±0.7)</td>
</tr>
</tbody>
</table>

But stroke/death rate for carotid stent was almost double that of endarterectomy.

Brott et al. CREST N Engl J Med 2010
Stroke Risk at 30 Days with Distal Filter Protection

1/5 to 1/3 of the strokes were non-ipsilateral

<table>
<thead>
<tr>
<th>CREST Results</th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Stroke</td>
<td>4.1%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Ipsilateral Stroke</td>
<td>2.0%</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

Pooled analysis: SAPPHIRE randomized and registry stent arms and CASES-PMS
ICSS MRI Subset

<table>
<thead>
<tr>
<th></th>
<th>Carotid stenting (n=124)</th>
<th>Carotid endarterectomy (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one new lesion</td>
<td>62 (50%)</td>
<td>18 (17%)</td>
</tr>
<tr>
<td>Single lesion</td>
<td>18 (15%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Multiple lesions</td>
<td>44 (35%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Location of lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral carotid circulation only</td>
<td>34 (27%)</td>
<td>14 (13%)</td>
</tr>
</tbody>
</table>

45% (28/62) of the new MRI lesions after CAS were non-ipsilateral.

Non-ipsilateral (contralateral carotid or vertebrobasilar) circulations only

6 (5%) 1 (1%)
TCAR: Transcervical Carotid Stent with Proximal Occlusion and Reversed Flow

ENROUTE® Transcarotid Neuroprotection & Stent System

Blood flow is reversed from the common carotid artery.

Working channel for interventional devices

Blood flow is returned to femoral vein

ENROUTE® Transcarotid Stent System (57cm)

Dynamic Flow Controller & Integrated 200µ Filter Hi / Low / Off

TCAR Tool Set
**Table IV.** DW-MRI results (percentage of mITT patients)

<table>
<thead>
<tr>
<th>DW-MRI parameters</th>
<th>All (n = 31)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects with DW-MRI lesion(s) pre- and postprocedure</td>
<td>1 (3.2%)</td>
</tr>
<tr>
<td>Number of subjects with new DW-MRI lesion(s) postprocedure</td>
<td>5 (16.1%)</td>
</tr>
<tr>
<td>Total number of new DW-MRI lesion(s) postprocedure</td>
<td>18</td>
</tr>
<tr>
<td>Number of new DW-MRI lesion(s) per subject postprocedure (min, max)</td>
<td>3.6 (2, 9)</td>
</tr>
</tbody>
</table>

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**Table II.** Results from diffusion-weighted magnetic resonance imaging (DW-MRI) evaluation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Transcervical (n = 31)</th>
<th>Transfemoral (n = 33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with new lesions</td>
<td>4 (12.90)</td>
<td>11 (33.33)</td>
<td>.03</td>
</tr>
<tr>
<td>No. of new lesions</td>
<td>4</td>
<td>13</td>
<td>.02</td>
</tr>
<tr>
<td>Localization of new lesions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral</td>
<td>4</td>
<td>11</td>
<td>.03</td>
</tr>
<tr>
<td>Contralateral</td>
<td>0</td>
<td>2</td>
<td>.16</td>
</tr>
</tbody>
</table>

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CEA Outcomes High Surgical Risk Patients
The obvious place to test TCAR

30-Day Stroke/Death

SVS Registry (n=6,370)*

High Surgical Risk CEA vs Standard Surgical Risk CEA

<table>
<thead>
<tr>
<th></th>
<th>Symptomatic</th>
<th>Asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Surgical Risk CEA</td>
<td>6.4%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Standard Surgical Risk CEA</td>
<td>3.9%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

p < .01  

p < .001
# ROADSTER 1 IDE
Outcomes Compare Favorably

TCAR 30-Day Outcomes on Par with CEA

<table>
<thead>
<tr>
<th></th>
<th>ROADSTER 1*</th>
<th></th>
<th>CREST**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High Surgical Risk</td>
<td>Standard Surgical Risk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pivotal (n=141)</td>
<td>Con’t Access (n=78)</td>
<td>All (n=219)</td>
</tr>
<tr>
<td>S/D/MI</td>
<td>3.5%</td>
<td>3.8%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.4%</td>
<td>1.3%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Death</td>
<td>1.4%</td>
<td>0.0%</td>
<td>0.9%</td>
</tr>
<tr>
<td>MI</td>
<td>0.7%</td>
<td>2.6%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Stroke &amp; Death</td>
<td>2.8%</td>
<td>1.3%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Cranial Nerve Injury (CNI)</td>
<td>0.7%</td>
<td>1.3%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Unresolved at 6 Mos</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

*Kwolek, LaMuraglia, Cambria. SVS Vascular Annual Meeting 2016

ROADSTER 2 Post-Approval Study: Currently Enrolling

- FDA-mandated open label, single arm, multi-center post-approval study
- Minimum of 600 patients; up to 100 sites
- Primary endpoint: rate of procedural success in patients treated per the FDA-approved labeling defined as:
  technical success in the absence of stroke, death or myocardial infarction at 30d
- Dedicated TCAR System = ENROUTE Neuroprotection + ENROUTE Stent

Principal Investigators: Peter Schneider, Vik Kashyap
ROADSTER 2: High Surgical Risk Patient Population

**Physiologic HSR Inclusion**
- Severe cardiac disease; severe COPD; chronic renal insufficiency
- Age ≥75

**Anatomic HSR Inclusion**
- Contralateral occlusion; bilateral or high or tandem stenoses
- Restenosis post CEA
- Permanent contralateral CNI
- Hostile neck
  - Irradiation
  - Radical neck dissection
  - Cervical spine immobility

**Exclusion: Common to CAS**
- Afib; recent valve or MI; bleeding
- Evolving stroke; neuro disorders
- Occlusion; ostial CCA or intracranial stenosis; string sign; previous stent

**Exclusion: Transcarotid**
- CCA disease at entry site
- <5cm clavicle to bifurcation
## ROADSTER 2: Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n=270</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥80</td>
<td>21.9%</td>
</tr>
<tr>
<td>Female</td>
<td>31.9%</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>28.3%</td>
</tr>
<tr>
<td>Physiologic Risk Factors only</td>
<td>32.5%</td>
</tr>
<tr>
<td>Anatomic Risk Factors only</td>
<td>44.3%</td>
</tr>
<tr>
<td>- Hostile Neck</td>
<td>17.0%</td>
</tr>
<tr>
<td>- Restenosis post CEA</td>
<td>20.3%</td>
</tr>
<tr>
<td>- Contralateral Occlusion</td>
<td>12.9%</td>
</tr>
<tr>
<td>Physiologic &amp; Anatomic Risk Factors</td>
<td>23.2%</td>
</tr>
</tbody>
</table>
## ROADSTER 2: Procedure Information

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ROADSTER 1 (N=219)</th>
<th>ROADSTER 2 (n=270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROADSTER 1 Investigators</td>
<td>N/A</td>
<td>26%</td>
</tr>
<tr>
<td>New Operators</td>
<td>N/A</td>
<td>74%</td>
</tr>
<tr>
<td>Enrollment by New Operators</td>
<td>N/A</td>
<td>58%</td>
</tr>
<tr>
<td>Skin-to-Skin Time (median)</td>
<td>70 mins</td>
<td>70 mins</td>
</tr>
<tr>
<td>Reverse Flow/Clamp Time (median)</td>
<td>9 mins</td>
<td>10 mins</td>
</tr>
<tr>
<td>Tolerance to High Flow</td>
<td>98.6%</td>
<td>99.3%</td>
</tr>
<tr>
<td>Tolerance to Low Flow</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Acute Technical Success</td>
<td>99.5%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Fluoro Time (median)</td>
<td>N/R</td>
<td>5 mins</td>
</tr>
<tr>
<td>Contrast Usage (median)</td>
<td>62 cc</td>
<td>40 cc</td>
</tr>
</tbody>
</table>
**ROADSTER 2:**
Endpoints to Date

**Patients Treated Per Protocol**

<table>
<thead>
<tr>
<th></th>
<th>n=252</th>
<th></th>
<th>n=227</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td></td>
<td><strong>Acute Device Success</strong></td>
<td>249</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Technical Success</strong></td>
<td>249</td>
</tr>
<tr>
<td><strong>30 Days</strong></td>
<td></td>
<td><strong>Procedural Success</strong></td>
<td>222</td>
</tr>
</tbody>
</table>

Procedural success:
Technical success in the absence of stroke, death or myocardial infarction at 30d
ROADSTER 2: Clinical Outcomes

Patients Treated Per Protocol

<table>
<thead>
<tr>
<th>Condition</th>
<th>ROADSTER 1 (n=203)</th>
<th>ROADSTER 2 (n=227)</th>
<th>ROADSTER 2 (n=252)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with 30-day F/U</td>
<td>Patients with 30-day F/U</td>
<td>All Patients</td>
</tr>
<tr>
<td>Stroke/Death/MI</td>
<td>6 (3.0%)</td>
<td>2 (0.9%)</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (0.5%)</td>
<td>2 (0.9%)</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>Death</td>
<td>2 (1.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>MI</td>
<td>3 (1.5%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Stroke/Death</strong></td>
<td><strong>3 (1.5%)</strong></td>
<td><strong>2 (0.9%)</strong></td>
<td><strong>2 (0.8%)</strong></td>
</tr>
<tr>
<td>CNI (permanent)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

**ROADSTER 2 Stroke in Asymptomatic Patients = 0.5%**

**ROADSTER 2 Stroke in Symptomatic Patients = 1.3%**
CEA-like outcomes with shorter learning curve than transfemoral-distal filter CAS

Gray WA et al. CAPTURE 2 Registry. JACC Cardiovasc Interv 2011;4:235-246

ROADSTER 1
29 Operators
S/D Rate = 2.3%*
N=219, Median=2, Mean=3.7

ROADSTER 2
49 New Operators
S/D Rate = 2.2%*
N=157, Median=2, Mean=3.3

*Includes patients with Major Protocol Deviations
ROADSTER 2 Interim Results

Conclusion

• Clinical outcomes in the ROADSTER 2 post-approval study are comparable to the those of ROADSTER 1 IDE Study.
  — >50% of enrollment in ROADSTER 2 is from operators with no prior TCAR experience

• ROADSTER 2 demonstrates comparable outcomes to CEA in high surgical risk patients.

• A dedicated stent and flow-reversal system can lead to the effective integration of TCAR for patients with carotid disease.
ROADSTER 2 Trial:
Transcervical access with reversed flow for proximal protection during CAS:
What have we learned so far?

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