Experience with a bilateral carotid filter protection during percutaneous aortic valve replacement

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Disclosure

Speaker name:
Axel Linke

I have the following potential conflicts of interest to report:

- [x] Consulting (Medtronic)
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [x] Other(s) Option Holder Claret Medical Inc.

- [ ] I do not have any potential conflict of interest
Stroke is just the tip of the iceberg...

...but can have far-reaching effects

- 68-100% of TAVR patients affected, most patients have multiple infarcts
- “Silent” infarcts are associated with:
  - 2-4-fold risk of future stroke
  - >3-fold risk of mortality
  - >2-fold risk of dementia
  - Cognitive decline

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6. Lansky, et al., EHJ 2015; May 19
8. Linke, et al., TCT 2014
9. Vahanian, TCT 2014
11. Sacco et al., Stroke 2013
12. Vermeer et al., Stroke 2003
The evidence to use embolic protection in TAVR

reduces ischemic brain volume
The Sentinel Trial

Patients with Severe Symptomatic Aortic Stenosis Undergoing TAVR

Patients Randomized (1:1:1)

n=363

Safety Cohort

SAFETY ARM
TAVR with Sentinel
(n=123)

TEST ARM
TAVR with Sentinel
(n=121)

CONTROL ARM
TAVR Only
(n=119)

Histopathology & Morphometry

Clinical Follow-Up

Serial MRIs (Baseline, Day 2-7 & Day 30)

Serial Neurocognitive Workup (Baseline, Day 30 & Day 90)

Imaging Cohort
The Sentinel Trial - Endpoints

- **Safety (Non-inferiority)**
  
  MACCE at 30 days compared to a historical performance goal
  - MACCE defined as All Cause Mortality, Stroke, AKI Class 3
  - As treated analysis utilizing patients from Safety Cohort

- **Efficacy (Superiority)**
  
  Reduction in median total new lesion volume in *protected* territories as assessed by DW-MRI at Day 2-7 post-procedure
  - Analysis performed using patients in imaging cohort
  - Analysis includes all patients that underwent MRI at both Baseline and 2-7 days (paired)
  - Success endpoint of 30% treatment effect
### The Sentinel Trial – Procedural Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control Arm (N=119)</th>
<th>Device Arm (N=121)</th>
<th>Safety Arm (N=123)</th>
<th>P-value(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sentinel Device Access</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radial</td>
<td>N/A</td>
<td>91.2%</td>
<td>95.0%</td>
<td>0.4918</td>
</tr>
<tr>
<td>Brachial</td>
<td>N/A</td>
<td>7.0%</td>
<td>4.2%</td>
<td></td>
</tr>
<tr>
<td>Both Filters Deployed</td>
<td>N/A</td>
<td>92.0%</td>
<td>96.6%</td>
<td>0.1570</td>
</tr>
<tr>
<td>At Least One Filter Deployed</td>
<td>N/A</td>
<td>99.1%</td>
<td>100.0%</td>
<td>0.4848</td>
</tr>
<tr>
<td><strong>Procedure Time(^2)</strong></td>
<td>74.2 ± 40.98</td>
<td>93.2 ± 51.53</td>
<td>81.7 ± 36.59</td>
<td>0.0075</td>
</tr>
<tr>
<td><strong>Fluoroscopy Time</strong></td>
<td>16.7 ± 11.50</td>
<td>20.9 ± 13.01</td>
<td>18.0 ± 10.78</td>
<td>0.0493</td>
</tr>
<tr>
<td><strong>TAVR Device Used</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.7176</td>
</tr>
<tr>
<td>Sapien XT</td>
<td>16.9%</td>
<td>17.5%</td>
<td>19.0%</td>
<td></td>
</tr>
<tr>
<td>Sapien 3</td>
<td>53.4%</td>
<td>55.8%</td>
<td>47.9%</td>
<td></td>
</tr>
<tr>
<td>CoreValve</td>
<td>5.9%</td>
<td>2.5%</td>
<td>3.3%</td>
<td></td>
</tr>
<tr>
<td>CoreValve Evolut R</td>
<td>23.7%</td>
<td>24.2%</td>
<td>29.8%</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) P-values are testing for statistical differences across randomized arms. Continuous data are compared using ANOVA; categorical data are compared using Fisher’s exact test.

\(^2\) Defined as time from first vascular access puncture to achievement of hemostasis at the TAVR access site.
The Sentinel Trial – Primary Safety Endpoint

30 Day MACCE Rates

- Historical Performance Goal: 18.3%
- Within Sentinel Trial: P = 0.40

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device Cohort</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td></td>
</tr>
</tbody>
</table>
# The Sentinel Trial – Primary Safety Endpoint

<table>
<thead>
<tr>
<th>30-day Clinical Outcomes</th>
<th>Control Arm</th>
<th>Safety + Device Arm</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any MACCE†</td>
<td>9.9% (11/111)</td>
<td>7.3% (17/234)</td>
<td>0.40</td>
</tr>
<tr>
<td>Death (all-cause)</td>
<td>1.8% (2/111)</td>
<td>1.3% (3/234)</td>
<td>0.65</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>9.1% (10/110)</td>
<td>5.6% (13/231)</td>
<td>0.25</td>
</tr>
<tr>
<td>Disabling</td>
<td>0.9% (1/109)</td>
<td>0.9% (2/231)</td>
<td>1.00</td>
</tr>
<tr>
<td>Non-disabling</td>
<td>8.2% (9/110)</td>
<td>4.8% (11/231)</td>
<td>0.22</td>
</tr>
<tr>
<td>AKI (Stage 3)</td>
<td>0%</td>
<td>0.4% (1/231)</td>
<td>1.00</td>
</tr>
<tr>
<td>TIA</td>
<td>0%</td>
<td>0.4% (1/231)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Sentinel Access Site Complications</strong></td>
<td>N/A</td>
<td>0.4% (1/231)</td>
<td>0.53</td>
</tr>
</tbody>
</table>
Sentinel – Primary Efficacy Endpoint

MRI New Lesion Volume (Protected Territories)

42.2% reduction

p = 0.33

<table>
<thead>
<tr>
<th>Study Arm</th>
<th>Count</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Whiskers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device</td>
<td>91</td>
<td>36.9</td>
<td>102.8</td>
<td>423.2</td>
<td>0, 1176</td>
</tr>
<tr>
<td>Control</td>
<td>98</td>
<td>34.3</td>
<td>178.0</td>
<td>482.5</td>
<td>0, 949</td>
</tr>
</tbody>
</table>
New Lesion Volume – Protected Territories
*Adjusted for Baseline lesion volume, Valve Type, Interaction of Valve Type and Treatment Arm*

<table>
<thead>
<tr>
<th></th>
<th>Mean Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protected Territories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Arm</td>
<td>162.8 mm³ (107.9, 245.5)</td>
<td>0.0248</td>
</tr>
<tr>
<td>Sentinel Arm</td>
<td>83.3 mm³ (55.0, 126.1)</td>
<td></td>
</tr>
</tbody>
</table>

New lesion volume in protected territories

- **49% reduction**
  
  (p = .0248)
Metaanalysis – CPD and Lesion Volume

**FIGURE 1** Meta-Analysis of Randomized Controlled Trials Investigating Claret (Claret Medical, Santa Rosa, California)
Cerebral Protection Filters

<table>
<thead>
<tr>
<th>CEP Better</th>
<th>WMD (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENTINEL</td>
<td>-44.0 (-132.6 to 44.7)</td>
<td>31.97</td>
</tr>
<tr>
<td>CLEAN-TAVI</td>
<td>-217.7 (-295.6 to -139.7)</td>
<td>33.76</td>
</tr>
<tr>
<td>MISTRAL-C</td>
<td>-78.3 (-153.2 to -3.5)</td>
<td>34.27</td>
</tr>
<tr>
<td></td>
<td>-114.4 (-218.2 to -10.5)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 80.1\% \quad p_{\text{heterogeneity}} = 0.007 \]

\[ Z = 2.16 \quad p\text{-value} = 0.031 \]

**shows Claret filters significantly reduce cerebral new lesion volume on MRI**

Latib and Pagnesi JACC 2017; 69(4):378-80
Results from SENTINEL multi-national randomized trial of n=363 TAVI patients with vs. without protection using Sentinel™ cerebral embolic protection system shows a significant reduction in periprocedural stroke (63%).

95% of SENTINEL patients were evaluated by neurologists
Clinical Events Committee included 2 stroke neurologists

SENTINEL trial. Data presented at Sentinel FDA Advisory Panel, February 23, 2017
The ULM Experience

- 802 all-comer consecutive TAVR patients at University of Ulm were prospectively enrolled
- A propensity-score analysis was done matching the 280 patients protected with Sentinel to 280 control patients

In multivariable analysis, **TAVR without cerebral emboli protection (p=0.044)** was the only independent predictor for stroke at 7-days
- **TAVR without cerebral emboli protection (p=0.028)** and STS score (<8 vs. ≥8) (p=0.021) were the only independent predictors for mortality and stroke at 7-days

Wöhrle J, Seeger J, et al. DGK Mannheim 2017; CSI-Ulm-TAVR Study clinicaltrials.gov NCT02162069
The Sentinel EPD is **safe**.

It’s use in TAVR leads to

- **a reduction in the volume of DW-MRI positive brain lesions** (by ~ 45%)

- **a potentially better preservation of neurocognitive function**

- **a potential reduction in clinical events (stroke and a composite of death and stroke)**
Conclusion

Given

- that every patient is at risk
  – independent of the valve type –
  
- that even small lesions might have a deep impact and

- that the CPD has been show to be safe,

it should be used in ALL TAVR cases.
Experience with a bilateral carotid filter protection during percutaneous aortic valve replacement

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