SORT OUT III

Perspectives on 18-Month Results
SORT OUT III Perspectives

- **Concerns with SORT OUT III Methodology:** The SORT OUT III study uses an unconventional methodology that raises questions regarding the reproducibility and viability of the results.

- **Inconsistency of Data for Cypher DES:** SORT OUT III shows unexpectedly low rates and inconsistent data for Cypher compared with nearly every other trial utilizing the Cypher stent.

- **SORT OUT III Results Are Short-Term Only:** The long-term deficiencies of Cypher demonstrated in multiple studies are not addressed by the short-term focus of SORT OUT III.

- **Consistency of Data for Endeavor DES:** While the SORT OUT III data are inconsistent for Cypher, the Endeavor outcomes in SORT OUT III reinforce the low and durable event rates for the Endeavor stent.
1. Positioned as a randomized “real-world” study yet nearly 60% (3344) of eligible patients were excluded in the analysis.

2. Unlike controlled trials with rigorous patient follow-up, SORT OUT III is dependent on patient records from a national database.

3. Investigators themselves—not an independent clinical events committee—determined and verified stent thrombosis (ST), target lesion revascularization (TLR), myocardial infarction (MI) and restenosis.

4. Procedure-related MIs were not captured, which may introduce bias because other studies utilizing these two stents have demonstrated a high rate of periprocedural MIs with Cypher and a low rate with Endeavor.

5. Differences in patient adherence to DAPT regimens were not reported despite the potential effect on safety outcomes.

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1 In-Hospital MI rates: Cypher 2.3%, BMS 1.5% (SIRIUS Trial); Cypher 3.5%, Endeavor 0.6% (ENDEAVOR III Trial)
SORT OUT III
Event Rates at 18 Months

- The MACE and MI rates in SORT OUT III exclude periprocedural MI.
- In ENDEAVOR III procedural MI = Cypher 3.5% vs. Endeavor 0.6% (p =0.042); therefore the impact on the MACE and MI rates in SORT OUT III is unknown.

Rasmussen K et al. Lancet, Published Online March 15, 2010

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Cypher: SORT OUT III TLR

Inconsistent Clinical Evidence

18 Months

1. Rasmussen K et al. Lancet, Published Online March 15, 2010
3. Klaus V et al., TCT 2009
4. Räber L et al., TCT 2009
Cypher: SORT OUT III MACE

*Inconsistent Clinical Evidence*

<table>
<thead>
<tr>
<th>Study</th>
<th>18 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>SORT OUT III</td>
<td>5.0%</td>
<td>10.0%</td>
</tr>
<tr>
<td>SORT OUT II</td>
<td>12.1%</td>
<td>8.4%</td>
</tr>
<tr>
<td>LEADERS</td>
<td></td>
<td>8.3%</td>
</tr>
<tr>
<td>SIRIUS</td>
<td></td>
<td>7.1%</td>
</tr>
<tr>
<td>Cypher Pooled</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N = Number of participants

1 Rasmussen K et al. Lancet, Published Online March 15, 2010
3 Klaus V et al., TCT 2009
4 Räber L et al., TCT2009
6 Caixeta A et al., JACC, 54 pp. 894-902, 2009.
Cypher: Long-Term Endpoint Increases

**MACE and TLR Increase from 1 – 5 Yr**

<table>
<thead>
<tr>
<th></th>
<th>SIRIUS N = 533</th>
<th>ARTS II N = 607</th>
<th>SIRTAX N = 503</th>
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</thead>
<tbody>
<tr>
<td><strong>MACE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 yr</td>
<td>8.3%</td>
<td>9.6%</td>
<td>8.3%</td>
</tr>
<tr>
<td>5 yr</td>
<td>20.3%</td>
<td>14.8%</td>
<td>24.4%</td>
</tr>
<tr>
<td><strong>TLR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 yr</td>
<td>4.5%</td>
<td>4.9%</td>
<td>9.1%</td>
</tr>
<tr>
<td>5 yr</td>
<td>8.6%</td>
<td>9.4%</td>
<td>14.9%</td>
</tr>
</tbody>
</table>

1 2 3 1 2 3

3. Räber L et al., TCT2009

* Total revascularization

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Cypher: Long-Term Endpoint Increases

**ARC Definite ST Increases from 1 – 5 Yr**

- **SIRIUS**
  - 1 yr: 0.8%
  - 5 yr: 1.2%
- **ARTS II**
  - 1 yr: 2.2%
  - 5 yr: 3.8%
- **SIRTAX**
  - 1 yr: 2.0%
  - 5 yr: 4.6%

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3. Räber L et al., TCT2009

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**Endeavor: SORT OUT III TLR**

**Consistent Clinical Evidence**

- **18 Months**
  - SORT OUT III (N = 1162): 6.0%
  - ENDEAVOR II (N = 592): 6.5%
  - ENDEAVOR III (N = 321): 7.0%
  - ENDEAVOR IV (N = 734): 5.9%
  - ENDEAVOR Japan (N = 97): 5.4%
  - E-Pooled (N = 1199): 6.2%
  - E-Five (N = 2054): 5.1%

- **24 Months**
  - SORT OUT III (N = 1162): 6.0%
  - ENDEAVOR II (N = 592): 6.5%
  - ENDEAVOR III (N = 321): 7.0%
  - ENDEAVOR IV (N = 734): 5.9%
  - ENDEAVOR Japan (N = 97): 5.4%
  - E-Pooled (N = 1199): 6.2%
  - E-Five (N = 2054): 5.1%

* ENDEAVOR III included angiographic follow-up in all patients.

ENDEAVOR Pooled Analysis: E I (5 yr), E II (5 yr), E II CA (5 yr), E III (5 yr), E IV (3 yr) and E pK (3 yr).
### Endeavor: SORT OUT III MACE

**Consistent Clinical Evidence**

<table>
<thead>
<tr>
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<th>18 Months</th>
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</tr>
</thead>
<tbody>
<tr>
<td>SORT OUT III</td>
<td>10.0%</td>
<td>9.9%</td>
</tr>
<tr>
<td>N = 1162</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENDEAVOR II</td>
<td>9.9%</td>
<td>9.2%</td>
</tr>
<tr>
<td>N = 592</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENDEAVOR III*</td>
<td>9.2%</td>
<td>9.8%</td>
</tr>
<tr>
<td>N = 321</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENDEAVOR IV</td>
<td>9.8%</td>
<td>9.8%</td>
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<tr>
<td>N = 734</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>7.8%</td>
<td>8.5%</td>
</tr>
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</tbody>
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ENDEAVOR Pooled Analysis: E I (5 yr), E II (5 yr), E II CA (5 yr), E III (5 yr), E IV (3 yr) and E pK (3 yr).
ENDEAVOR Pooled Analysis

TLR and ARC Def/Prob ST From 1 – 5 Yr

TLR

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate</th>
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<tr>
<td>1 yr</td>
<td>5.4%</td>
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<td>5 yr</td>
<td>7.0%</td>
</tr>
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</table>

ARC Definite/Probable ST

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate</th>
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</thead>
<tbody>
<tr>
<td>1 yr</td>
<td>0.6%</td>
</tr>
<tr>
<td>5 yr</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

N = 2132
SORT OUT III Perspectives

- **Concerns with SORT OUT III Methodology:** The SORT OUT III study uses an unconventional methodology that raises questions regarding the reproducibility and viability of the results.

- **Inconsistency of Data for Cypher:** SORT OUT III shows unexpectedly low rates and inconsistent data for Cypher compared with nearly every other trial utilizing the Cypher stent.

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Endeavor: Durable TLR Rates
Real-World Experience Consistent with Pooled Analysis

Cumulative Incidence of TLR (%)

Days 0 180 360 540 720 730 900 1080 1260 1440
No. at Risk 2133 2130 2061 1939 1895 1557 1169 1150 1015 858
% CI 0.1 1.8 5.4 5.8 6.2 6.2 6.5 6.7 6.7 6.7
No. at Risk 2116 2113 2046 1974 1924 1816
% CI 0.0 2.3 4.5 4.8 5.0 5.0

ENDEAVOR Pooled Analysis: E I (5 yr), E II (4 yr), E II CA (4 yr), E III (3 yr), E IV (2 yr) and E pK (2 yr).
The 2-year follow-up rate for Pooled Analysis was measured at 720 days and for E-Five at 730 days.
Endeavor: Low Rates of ARC Def/Prob ST
Real-World Experience Consistent with Pooled Analysis

ENDEAVOR Pooled Analysis: E I (5 yr), E II (4 yr), E II CA (4 yr), E III (3 yr), E IV (2 yr) and E pK (2 yr).
The 2-year follow-up rate for Pooled Analysis was measured at 720 days and for E-Five at 730 days.

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