When Can Standard EVAR Be Safely & Durably Performed in Patients with Challenging Anatomies?

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I have the following potential conflicts of interest to report:

Medtronic
WL Gore
Philips
Endologix
Arsenal AAA
• Proximal aneurysm neck is the Achilles heel of EVAR
  – Essential for proper fixation and sealing
  – Most frequent constraint for EVAR

• Extensive research has shown that hostile proximal neck anatomy challenges a durable seal over time
Background

- Systematic reviews have compared patients treated outside neck IFU with patients treated per manufacturer’s recommendations.

  **Type I endoleaks** 4.5x more likely at 1-year in hostile neck anatomy patients \((P=0.01)\)

  **ARM** risk 9x greater at 1-year in hostile neck anatomy patients \((P=0.013)\)

\(^1\)Antoniou GA, et al. JVS 2013;57(2):527-38
Question that Remains

When can standard EVAR be safely and durably performed in patients with hostile necks?
On- vs. Off-Label Analysis of Endurant

Considering that implanting endografts outside IFU is not uncommon in global daily practice

It seems important to know how off-label use affect outcomes

To address this, an On- vs Off-label analysis was performed with ENGAGE, a large, real-world registry providing real-life data
Insights from the ENGAGE Registry

Largest Contemporary EVAR Registry with single stent graft (Endurant)

- N=1263 pts; Prospective/Consecutive Enrollment (2009-2010)
  - Initiated to evaluate Endurant in real-world population
- 79 Centers, across 30 Countries
  - Diverse patient and physician population
- Adherence to IFU advised; Off-IFU pts permitted
- High-Quality Data
  - 100% data management review
  - Independent data monitoring (100% endpoints)
  - Independent Clinical Event Committee
Challenging Patient Population

- ~80% due to proximal neck parameters
- Increased risk of graft displacement over time
- Patients unique to Registry; not allowed in Regulatory Trials
- Challenging patients, historically underserved (N=131)
- Patients at increased risk for proximal failure
### ENGAGE Registry

**On- vs. Off-Label Analysis**

<table>
<thead>
<tr>
<th>Initial Implant</th>
<th>On-Label</th>
<th>Off-Label</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful Delivery and Deployment</td>
<td>99.4% (1042/1048)</td>
<td>99.5% (214/215)</td>
<td>0.847</td>
</tr>
</tbody>
</table>

Early technical success similar between On- and Off-Label cohorts.
## Main Body Migration through 4 years similar between On- and Off-Label cohorts

<table>
<thead>
<tr>
<th></th>
<th>On-Label</th>
<th>Off-Label</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Body Migration</td>
<td>0.1%</td>
<td>0.0%</td>
<td>0.651</td>
</tr>
</tbody>
</table>

Through 4 Years

ENGAGE Registry

On- vs. Off-Label Analysis
ENGAGE Registry
On- vs. Off-Label Analysis

Freedom from Type Ia: All Pts

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Freedom Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 YR</td>
<td>97.8%</td>
</tr>
<tr>
<td>2 YR</td>
<td>97.3%</td>
</tr>
<tr>
<td>3 YR</td>
<td>96.7%</td>
</tr>
<tr>
<td>4 YR</td>
<td>96.0%</td>
</tr>
</tbody>
</table>

# of patients at risk at beginning of interval

1226  1128  977  870
Engage Registry
On- vs. Off-Label Analysis

Freedom from Type Ia: On-IFU

- 1 YR: 98.5%
- 2 YR: 98.2%
- 3 YR: 97.7%
- 4 YR: 97.0%

Freedom from Type Ia: Off-IFU

- 1 YR: 94.6%
- 2 YR: 93.1%
- 3 YR: 91.9%
- 4 YR: 91.2%

4 Yrs
97.0%
vs.
91.2%
p<0.0001

# of patients at risk at beginning of interval:
On-IFU:
1038
935
808
724

Off-IFU:
225
193
169
146
**ENGAGE Registry**

**On- vs. Off-Label Analysis**

<table>
<thead>
<tr>
<th>Through 4 Years</th>
<th>On-Label</th>
<th>Off-Label</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Endovascular Procedures</td>
<td>10.7% (109/1023)</td>
<td>13.0% (27/208)</td>
<td>0.330</td>
</tr>
</tbody>
</table>

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<tr>
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<th>Off-Label</th>
<th>P-Value</th>
</tr>
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<tr>
<td>Secondary Endovascular Procedures to correct Type I/III endoleaks</td>
<td>3.1% (32/1023)</td>
<td>6.7% (14/208)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Through 4 Years in Off-Label cohort:
- ✓ 8pts required 2nd endo procedures for Type Ia endoleaks,
- ✓ 5pts for Type Ib endoleaks,
- ✓ 1pt for combination Type Ia/Ib endoleaks
## ENGAGE Registry
### On- vs. Off-Label Analysis

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<th>Off-Label</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aneurysm Rupture</strong></td>
<td>0.9% (9/1023)</td>
<td>0.9% (2/208)</td>
<td>0.909</td>
</tr>
</tbody>
</table>

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<th>Off-Label</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Conversion to Open Surgery</strong></td>
<td>1.2% (12/1023)</td>
<td>0.5% (1/208)</td>
<td>0.373</td>
</tr>
</tbody>
</table>

Aneurysm Rupture and Conversion to Open Surgery similar between On- and Off-Label cohorts
Through 4 Years, Freedom from ARM similar between On- and Off-Label cohorts

Freedom from Aneurysm-Related Mortality
through 4 years

98.5% On-Label
97.7% Off-Label

p-value 0.331

Aneurysm-Related Deaths

0 – 30d: 16
31d – 1 year: 2
1 -2 year: 1
2 – 3 year: 0
3 – 4 year: 1
ENGAGE Registry

Sac dynamics

4Yr AAA Sac Dynamics

- 

N=582 pts
90 pts Off-IFU (15.5%)

- Decrease 60.3%
- Stable 28.9%
- Increase 10.8%

89.2% Decrease or stable at 4 years
ENGAGE Registry
On- vs. Off-Label Analysis

AAA Sac Dynamics
Percent of Patients \textit{without} AAA Enlargement

Schanzer, Circ. 2011

Lack of AAA Sac Enlargement in On- and Off-Label ENGAGE Patients Encouraging
In Summary

• Through 4 years, there’s no outcome differences between On- and Off-Label pts treated with Endurant in terms of:
  – Delivery and Deployment
  – Migrations
  – 2nd procedures Overall
  – Ruptures
  – Conversions
  – Aneurysm-Related Mortality

• In Off-Label patients, a difference is noted in Type Ia endoleaks and 2nd procedures to treat these
Conclusions

- ENGAGE represents a real-world patient *and* real-world practice population
  - 17% pts are Off-Label (N=215); ~80% due to proximal neck characteristics
- Endurant demonstrates strong performance in both On- and Off-Label patients; however, Off-Label patients require more 2nd procedures to treat type Ia endoleaks.
- With Off-Label patients, physicians must balance risk of standard EVAR versus alternative therapies; treating patients On-Label is encouraged.
- When treating patients Off-Label, it is important to evaluate each device’s performance Off-IFU as there are device-specific differences.
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