Unparalleled clinical data outcome from one AAA device and expanded treatment options with approval

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Agenda

- 5 years Results of ENGAGE
- CHEVAR =CE marked procedure Endurant /V12 Advanta
- Endoanchoring
Disclosures

• PI of ENGAGE
• Consultancy and Research Funding
ENGAGE Global Registry

- 1,263 Patients
- 30 Countries
- 6 Continents

Clinical Follow up
- 90% after 5 yrs.

Imaging Follow up
- >75% after 5 yrs.
Patients Consecutively Enrolled

Follow-up:
30-day, Annual Visits Through 10 Years

Extensive Monitoring On-going

100% Data Management Review

Independent Data Monitoring (100% Endpoints)

Independent Clinical Event Committee

High Quality Data
ENGAGE – Challenging Baseline Characteristics

78.2% of Outside IFU Patients Had Challenging Proximal Neck Anatomical Characteristics
**ENGAGE – Freedom From All-Cause Mortality**

<table>
<thead>
<tr>
<th>Time from Initial Procedure</th>
<th>No. at Risk</th>
<th>No. of Events</th>
<th>No. Censored</th>
<th>Kaplan-Meier Estimate</th>
<th>Peto Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 30 days</td>
<td>1263</td>
<td>16</td>
<td>4</td>
<td>0.987</td>
<td>0.003</td>
</tr>
<tr>
<td>1 month – 1 year</td>
<td>1243</td>
<td>79</td>
<td>14</td>
<td>0.924</td>
<td>0.008</td>
</tr>
<tr>
<td>1 – 2 year</td>
<td>1150</td>
<td>80</td>
<td>72</td>
<td>0.859</td>
<td>0.010</td>
</tr>
<tr>
<td>2 – 3 year</td>
<td>998</td>
<td>76</td>
<td>29</td>
<td>0.793</td>
<td>0.012</td>
</tr>
<tr>
<td>3 – 4 year</td>
<td>893</td>
<td>70</td>
<td>44</td>
<td>0.729</td>
<td>0.014</td>
</tr>
<tr>
<td>4 – 5 year</td>
<td>779</td>
<td>70</td>
<td>262</td>
<td>0.674</td>
<td>0.017</td>
</tr>
</tbody>
</table>

**FF ACM 67.4% ± 1.96*1.7%**
**ENGAGE – Freedom From Aneurysm Related Mortality**

- **Kaplan-Meier Estimates for Aneurysm-related Mortality**
  - **No. at Risk**: 1263, 1150, 998, 893, 779, 463
  - **No. of Events**: 16, 3, 1, 1, 3, 1
  - **No. Censored**: 4, 90, 151, 104, 111, 315
  - **Kaplan-Meier Estimate**: 0.987, 0.985, 0.984, 0.983, 0.979, 0.978
  - **Peto Standard Error**: 0.003, 0.004, 0.004, 0.004, 0.005, 0.005

- **FF ARM 97.8% ± 1.96*0.5%**
Freedom From All-Cause Mortality Comparison in EVAR 1

FF ARM > 74 %

* Meta-analysis of Individual-patient Data from EVAR-1, DREAM, OVER and Ace Trials Comparing Outcomes of Endovascular or Open Repair For Abdominal Aortic Aneurysm Over 5 years. J.T. Powell et al. Br J of Surg. 2017
ENGAGE – Freedom From Conversion to Open Surgery

FF Conversion 97.9% ± 1.96*0.6%

<table>
<thead>
<tr>
<th>Time from Initial Procedure</th>
<th>At 1 Year</th>
<th>At 2 Year</th>
<th>At 3 Year</th>
<th>At 4 Year</th>
<th>At 5 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conversion</td>
<td>0.6% (7/1263)</td>
<td>0.3% (3/1150)</td>
<td>0.1% (1/998)</td>
<td>0.2% (2/893)</td>
<td>0.8% (6/779)</td>
</tr>
</tbody>
</table>
ENGAGE – Type Ia Endoleak On-label vs. Off-Label

<table>
<thead>
<tr>
<th></th>
<th>On-Label Subjects</th>
<th>Off-Label Subjects</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At 5 Year</td>
<td>At 5 Year</td>
<td></td>
</tr>
<tr>
<td>N = 1038</td>
<td></td>
<td>N = 225</td>
<td></td>
</tr>
<tr>
<td>Type Ia Endoleak</td>
<td>1.2% (5 / 425)</td>
<td>3.9% (3 / 76)</td>
<td>0.106</td>
</tr>
</tbody>
</table>
ENGAGE – Freedom From Aneurysm Rupture

Kaplan-Meier Estimates for Aneurysm Rupture

<table>
<thead>
<tr>
<th>Time from Initial Procedure</th>
<th>0-30 days</th>
<th>1 day – 1 year</th>
<th>1 year – 2 year</th>
<th>2 year – 3 year</th>
<th>3 year to 4 year</th>
<th>4 year – 5 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at Risk¹</td>
<td>1263</td>
<td>1243</td>
<td>1149</td>
<td>997</td>
<td>891</td>
<td>775</td>
</tr>
<tr>
<td>No. of Events</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>No. Censored²</td>
<td>20</td>
<td>92</td>
<td>150</td>
<td>104</td>
<td>111</td>
<td>314</td>
</tr>
<tr>
<td>Kaplan-Meier Estimate³</td>
<td>1</td>
<td>0.998</td>
<td>0.996</td>
<td>0.994</td>
<td>0.988</td>
<td>0.986</td>
</tr>
<tr>
<td>Peto Standard Error</td>
<td>0.000</td>
<td>0.001</td>
<td>0.002</td>
<td>0.002</td>
<td>0.004</td>
<td>0.004</td>
</tr>
</tbody>
</table>

FF Rupture 98.6% ± 1.96*0.4%
ENGAGE – Freedom From Secondary Procedure

Kaplan-Meier Estimates for Secondary Endovascular Procedure

<table>
<thead>
<tr>
<th>Time from Initial Procedure</th>
<th>0 - 30 days</th>
<th>1 month – 1 year</th>
<th>1 year – 2 year</th>
<th>2 year – 3 year</th>
<th>3 year – 4 year</th>
<th>4 year – 5 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at Risk(^1)</td>
<td>1257</td>
<td>1214</td>
<td>1081</td>
<td>921</td>
<td>804</td>
<td>685</td>
</tr>
<tr>
<td>No. of Events</td>
<td>25</td>
<td>51</td>
<td>21</td>
<td>22</td>
<td>19</td>
<td>22</td>
</tr>
<tr>
<td>No. Censored(^2)</td>
<td>18</td>
<td>82</td>
<td>139</td>
<td>95</td>
<td>100</td>
<td>258</td>
</tr>
<tr>
<td>Kaplan-Meier Estimate(^3)</td>
<td>0.98</td>
<td>0.938</td>
<td>0.919</td>
<td>0.896</td>
<td>0.874</td>
<td>0.843</td>
</tr>
<tr>
<td>Peto Standard Error</td>
<td>0.004</td>
<td>0.007</td>
<td>0.008</td>
<td>0.010</td>
<td>0.012</td>
<td>0.015</td>
</tr>
</tbody>
</table>

FF Sec. Proc. 84.3% ± 1.96*1.4%
ENGAGE shows in absolute figures an approximate 10% benefit in Freedom From Secondary Procedure than what was reported in EVAR-1.
ENGAGE – Freedom From Secondary Procedures
On-Label vs Off-Label

FF Sec. Proc. On-label 84.3%
FF Sec. Proc. Off-Label 84.1%
p-value = 0.8020
ENGAGE – AAA Diameter Change

Durability in Real-world Patients
89.4% of AAA Show a Sac Decrease/Stable

- 61.4% Decrease
- 28.0% Stable
- 10.6% Increase
Summary of results at 5 years

- **FF From Aneurysm Related Mortality**: 97.8%
- **FF from Aneurysm Rupture**: 98.6%
- **FF From Secondary Procedure**: 84.3%
- **Rate AAA Sac Diameter Stable or Decrease**: 89.4%
Discussion - implications

• The ENGAGE registry demonstrates how EVAR evolution has contributed to improved patients outcomes

• Large real world registries as ENGAGE has the potential to clarify how to customize patient follow-up, which will increase the cost-effectiveness of EVAR.

• Longer-term data will be needed to see if durability is maintained (ENGAGE follow-up will extend to 10 years)
HOSTILE PROXIMAL NECK PREDICTS CHALLENGES

4.5x

Type I endoleaks 4.5x more likely at 1-year after EVAR in hostile proximal neck anatomy (P = .010)

9x

Aneurysm-related mortality risk 9x greater in hostile neck anatomy at 1-year (P=.013)

Meta-Analysis of 7 major studies in EVAR by Antoniou et al\textsuperscript{1} compared outcomes in hostile vs. friendly neck anatomies (total patients N = 1559)

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>EndoGrafts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torsello et al, 2011</td>
<td>177</td>
<td>Endurant™</td>
</tr>
<tr>
<td>AbuRahma et al, 2010</td>
<td>238</td>
<td>AneuRx™, Excluder™<em>, Zenith™</em>, Talent™</td>
</tr>
<tr>
<td>Hoshina et al, 2010</td>
<td>129</td>
<td>Excluder™<em>, Zenith™</em></td>
</tr>
<tr>
<td>Abbruzzese et al, 2008</td>
<td>565</td>
<td>AneuRx™, Excluder™<em>, Zenith™</em></td>
</tr>
<tr>
<td>Choke et al, 2006</td>
<td>147</td>
<td>Talent™, Zenith™<em>, Excluder™</em>, AneuRx™</td>
</tr>
<tr>
<td>Fulton et al, 2006</td>
<td>84</td>
<td>AneuRx™</td>
</tr>
<tr>
<td>Fairman et al, 2004</td>
<td>219</td>
<td>Talent™</td>
</tr>
</tbody>
</table>

\textsuperscript{1} Antoniou GA et al. JVS. 2013;57(2):527-38
POSSIBLE SOLUTIONS

• EXTEND PROXIMALLY TO CREATE A NEW SEALING ZONE

“Chimney”

FEVAR

• CREATE AN ENDOVASCULAR SUTURE LINE
To build more proximally endovascularly, current options: chEVAR

- On-label CE Mark (Endurant + BECS)
- Upper extremity access required
- Renal manipulation
Potential advantages of ChEVAR

- Approved Indication
- May Increase Proximal Seal Zone
- Cost Effective / Device Cost
- Off the Shelf Product Availability
- Flexible Aortic Stent Graft System
- Low Profile Devices
- Urgent/emergent availability*
- Angled neck
- Challenging access vessels

* The safety and effectiveness of the Endurant™ II/IIs stent graft system has not been evaluated in patients who require emergent aneurysm treatment
PERICLES - Road Toward Standardization

Collected World Experience About the Performance of the Snorkel/Chimney Endovascular Technique in the Treatment of Complex Aortic Pathologies

*The PERICLES Registry*

Konstantinos P. Donas, MD,* Jason T. Lee, MD,† Mario Lachat, MD,‡ Giovanni Torsello, MD, PhD,§ and Frank J. Veith, MD;¶ on behalf of the PERICLES investigators

517 patients from 13 international centers

Non-industry funded Registry

(50.2% Endurant™ stent graft)

PERICLES study

- Max diameter: 65.9 ± 21.6 mm
- Infrarenal neck diameter: 26.4 ± 4.8 mm
- Infrarenal neck length: 4.8 ± 7.4 mm
- Neck length/seal zone changed to: 21.1 + 12.7 mm

Donas K et. al; Ann Surg. 2015 Sep;262(3):546-53
## PERICLES study- MAIN OUTCOMES

517 patients from 13 international centres

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean follow up</td>
<td>17.1 months</td>
</tr>
<tr>
<td>Intra-op type Ia endoleak:</td>
<td>7.9%</td>
</tr>
<tr>
<td>Persistent intra-op type Ia endoleak</td>
<td>2.9%</td>
</tr>
<tr>
<td>Technical Success</td>
<td>97.1%</td>
</tr>
<tr>
<td>Chimney-graft patency</td>
<td>94.1%</td>
</tr>
</tbody>
</table>

- Results due to combination of devices and 3 or 4 vessel ChEVAR
- Need for standardized approach

Donas K et. al; *Ann Surg.* 2015 Sep;262(3):546-53
Pericles study - SUMMARY

• ChEVAR is a valid off-the-shelf alternative in the treatment of complex EVAR and reinforces the need for standardization of the technique

• Reproducible results for **13 European** and **US** centers and > 500 treated patients with high intraoperative success

• Low incidence of persistent or new onset of type 1a endoleaks after ChEVAR in case of a new neck length of approximately **20 mm**

• Results due to combination of devices.

• ChEVAR is a safe and effective alternative endovascular treatment for juxtarenal pathologies.

Donas K et. al; *Ann Surg.* 2015 Sep;262(3):546-53
PROTAGORAS study

The PROTAGORAS study to evaluate the performance of the Endurant stent graft for patients with pararenal pathologic processes treated by the chimney/snorkel endovascular technique.


128 patients with pararenal pathologies and the intention to treat by Endurant™ and Atrium Advanta™* V12¹ as chimney graft

- Standardized device combination and protocol
- Study endpoints include:
  - Sac diameter regression
  - Chimney graft patency
  - Chimney graft-related reinterventions

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative proximal neck diameter</td>
<td>24.9 ± 3.7 mm</td>
</tr>
<tr>
<td>Preoperative suprarenal neck angulation</td>
<td>22.8 ± 22.6°</td>
</tr>
<tr>
<td>Preoperative proximal neck length</td>
<td>4.7 ± 3.2 mm</td>
</tr>
<tr>
<td>Postoperative new neck length after use of chimney grafts</td>
<td>18.7 ± 6.3 mm</td>
</tr>
</tbody>
</table>

TV per patient | 1.5
Technical success | 100%
30 day mortality | 0.08%

The PROTAGORAS study

Primary chimney graft patency **95.7%** through 24.6 months

Freedom from Chimney graft reinterventions **93.1%** through 24.6 months

NEW ONSET TYPE IA ENDOLEAK **1.6%**

The PROTAGORAS study

90.6 % patients had reduced or stable AAA diameter

Sac regression: 64.8 → 60.1mm, p <0.001

Sac behaviour is comparable to Endurant performance in ENGAGE Registry

The PROTAGORAS study

- Standard use of the Endurant™ stent graft system for ChEVAR and Advanta™* V12™* as chimney graft in 128 patients is associated with high Technical Success, significant Aneurysm Sac Regression and low incidence of Secondary Procedures.

- Standardization of device combinations, creation of a new proximal neck length of >15 mm, and meticulous follow-up seem to be the keys to achieving durable results for patients with pararenal diseases treated by ChEVAR.

- Reproducible experience from other centers is needed to establish this total endovascular alternative therapeutic option.

TM*=MAQUET Cardiovascular, LLC; Third party brands are trademarks of their respective owners
WHY SHOULD WE REINFORCE SEALING AND FIXATION INFRARENALLY?
Establishes the strength of a sutured anastomosis

More competent proximal seal and fixation by increasing apposition between the aorta and the endograft
Clinical History of Endoanchors

- First Human Implant: 2005 (Drs Deaton, Ohki, Condado)
- STAPLE – 1: 2006-2007, 21 pts
- STAPLE – 2: 2007-2009, 155 patients (5yr IDE f/u with 0% type Ia)
- ANCHOR Registry – start 2012, EU/US, >830 pts to date, 5yr f/u planned
- Total world experience >10,000 cases / >50,000 EndoAnchors implanted
A more competent proximal seal enhances AAA remodeling

In a propensity-matched study design, significantly greater AAA regression at 2 years post-EVAR

Methodology
- Pre-EVAR CTs by core lab
- 2 cohorts:
  - 99pts EVAR
  - 99pts EVAR+EndoAnchor
- Propensity matching on 19 variables

P-value = 0.01

Promotes increased rate of AAA sac regression
**Clinical Evaluation**
ANCHOR Registry Short Neck Cohort

- Anchor Registry Patients
  - Primary
  - Revision

- Endurant Stent Graft
- Other Devices

**Baseline Anatomical Characteristics per Core Lab**
- **Infrarenal Diameter:** 25.7 mm
- **Infrarenal Angulation:** 20.6°
- **Neck Length:** 6.86 mm
- **Aneurysm Diameter:** 57.7 mm
- **Avg Neck Calcium Thickness:** 1.31 mm
- **Avg Neck Thrombus Thickness:** 0.85 mm

70 Endurant Patients with Short Necks (<10 mm down to 4 mm)
Endurant + Heli-FX Short Neck Cohort (N=70)

<10mm down to 4mm length*
19 – 32mm diameters
≤ 60° infrarenal angulation
Femoral-only approach
No renal instrumentation
Off-the-shelf
18 – 20 Fr OD

* Core Lab defined neck length: length over which neck diameter remains within 10% of infrarenal diameter
Endurant + Heli-FX Short Neck Cohort (N=70)

Initial Implant Procedure

<table>
<thead>
<tr>
<th></th>
<th>148</th>
<th>17</th>
<th>35</th>
<th>5.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. duration of Procedure (min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avg. time to EndoAnchor implant (min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avg. Fluoro Time (min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avg. number of EndoAnchor implants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Technical Success: 88.6% (62/70)
- Procedural Success: 97.1% (68/70)

<table>
<thead>
<tr>
<th></th>
<th>1 month</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1a Endoleak</td>
<td>6.8% (4/59)</td>
<td>1.9% (1/53)</td>
</tr>
<tr>
<td>Endograft Migration</td>
<td>N/A</td>
<td>0.0% (0/41)</td>
</tr>
<tr>
<td>2nd Endo Procedure</td>
<td>2.9% (2/70)</td>
<td>4.7% (3/64)*</td>
</tr>
</tbody>
</table>

Sac behavior at 12 months

- Increase 0.0%
- Stable 57.4%
- Decrease 42.6%

* 1.6% (N=1) 2nd Procedure to treat proximal neck
Endurant + Heli-FX Short Neck Cohort (N=70)

<table>
<thead>
<tr>
<th>Kaplan-Meier Estimates</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedom from ACM</td>
<td>92.7%</td>
</tr>
<tr>
<td>Freedom from ARM</td>
<td>94.3%</td>
</tr>
<tr>
<td>Freedom from 2\textsuperscript{nd} Procedures</td>
<td>95.4%</td>
</tr>
<tr>
<td>Freedom from rupture</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adverse Events through 12 months</th>
<th>Patients with Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>EndoAnchor Implant-Related SAE</td>
<td>0/70</td>
</tr>
<tr>
<td>Aneurysm Rupture</td>
<td>0/64</td>
</tr>
<tr>
<td>AAA-Related Mortality</td>
<td>4/68</td>
</tr>
<tr>
<td>Open Surgical Conversion</td>
<td>0/64</td>
</tr>
</tbody>
</table>

Very good early clinical outcomes in a challenging patient population
Arguments Pro: Endurant + Heli-FX in Short Necks

<table>
<thead>
<tr>
<th>Device Availability</th>
<th>Access</th>
<th>Complexity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Off-the-shelf</td>
<td>Endurant 18/20 Fr OD</td>
<td>No upper extremity access required</td>
</tr>
<tr>
<td>Available for symptomatic or rupture cases</td>
<td>Heli-FX 16 Fr OD</td>
<td>Less time under general anesthesia for highly comorbid patients</td>
</tr>
<tr>
<td></td>
<td>FEVAR 23.4 Fr OD</td>
<td></td>
</tr>
</tbody>
</table>
Arguments Pro: Endurant + Heli-FX in Short Necks

**Contrast and Radiation**
- Low fluoro times means less radiation exposure
- Low contrast use equals less renal insult

**Economics**
- No renovisceral stents leads to less devices used
- Shorter procedure times
- Fewer reinterventions equates to lower overall patient costs

**Encouraging 1-Year Outcomes**
- 1.9% type Ia (N=1)
- No conversions or ruptures
- 1.6% proximal-neck 2nd procedures
Conclusions

• Standard EVAR = safe and effective solution to treat standard anatomy

• In complex anatomies we need to tailor the right endovascular solution among the existing complementary options, considering multiple factors (anatomy, comorbidities, cost, etc.)

• CHEVAR and Endoanchoring seems to be safe and effective
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