Real World Evidence
Eluvia DES

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Disclaimer

- IMPORTANT INFORMATION: These materials are intended to describe common clinical considerations and procedural steps for the on-label use of referenced technologies as well as current standards of care for certain conditions. Of course, patients and their medical circumstances vary, so the clinical considerations and procedural steps described may not be appropriate for every patient or case. As always, decisions surrounding patient care depend on the physician’s professional judgment in light of all available information for the case at hand.

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- Results from case studies are not necessarily predictive of results in other cases. Results in other cases may vary.
Disclosures

Speaker name: G. Torsello

I have the following potential conflicts of interest to report:

X Consulting: Boston Scientific, Cook, Cordis, Gore, Medtronic
   Employment in industry
   Stockholder of a healthcare company
   Owner of a healthcare company
   Other(s)
Background

• BSC’s RCT programme has shown the clinical benefit using DCB and DES devices for patients undergoing fem-pop procedures.

• RCTs enroll a selected group of patients, in terms of both clinical and imaging criteria.

• Their results cannot be fully extrapolated to daily practice treating “all-comers” population.

• Systematic registries, with robust data capture, can compliment RCT data, and provide supporting evidence of generalizability.
Auckland Registry

- Single center audit of “real world” experience with Eluvia in femoropopliteal intervention
- All patients had at least 2 years follow-up (treated March 2016 – October 2017)

- N = 51
- 105mm mean lesion length
- 53% CTOs
- mean CTO length 90.1mm
- 51% with significant calcification (PACSS ≥ 3)
Auckland Registry

• Concomitant ipsilateral limb intervention – 20 cases (39.2%), 17 cases tibial

• No stent fractures on follow up

• No “halo” on Duplex US to 2 years and beyond

• 2-year all cause mortality 3/51 (5.8%) – suicide, heart failure, sepsis

Results

<table>
<thead>
<tr>
<th></th>
<th>1 Month</th>
<th>6 Months</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Patency</td>
<td>98.0%</td>
<td>98.0%</td>
<td>94.0%</td>
<td>93.8%</td>
</tr>
<tr>
<td></td>
<td>(50/51)</td>
<td>(49/50)</td>
<td>(47/50)</td>
<td>(45/48)</td>
</tr>
<tr>
<td>Freedom from CD-TLR</td>
<td>98.0%</td>
<td>98.0%</td>
<td>98.0%</td>
<td>93.8%</td>
</tr>
<tr>
<td></td>
<td>(50/51)</td>
<td>(49/50)</td>
<td>(49/50)</td>
<td>(45/48)</td>
</tr>
</tbody>
</table>
DESAFINADO

- N=64
- 193 mm mean lesion length
- 52% severely calcified (PARC)
- 48% total occlusion
- 58% TASC C/D
- 30% extending into P2/P3
- 70% total lesion coverage

- 84% Critical Limb Ischemia
- 78% Diabetes Mellitus
- 17% Dialysis dependent

12 Month Results

<table>
<thead>
<tr>
<th>12 Months</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Patency</td>
<td>84%</td>
</tr>
<tr>
<td>Freedom from TLR</td>
<td>92%</td>
</tr>
<tr>
<td>Amputation-free Survival</td>
<td>80%</td>
</tr>
<tr>
<td>(Major)</td>
<td></td>
</tr>
<tr>
<td>Limb Salvage</td>
<td>93%</td>
</tr>
<tr>
<td>Complete Wound Healing</td>
<td>80%</td>
</tr>
</tbody>
</table>

Note: Kaplan-Meier Estimates. a Duplex ultrasound peak systolic velocity ratio ≤2.4

PP = 84 %
REGAL Registry

Complimentary / confirmatory real world, daily practice use, multi-centre registry with primarily EU centres not in EMINENT RCT

- N=291
- **98.4 mm mean lesion length**
- 49.8% occlusions
- 37.2% Rutherford-Becker Class 4-6
- 48.5% diabetes mellitus
- 15.1% Renal insufficiency
CD-TLR: Clinically-Driven Target Lesion Revascularization; Subjects event-free at 760 days or later are censored at greater than 760 days. Intervals are end inclusive, e.g. interval 182 is defined as 120-182 days, inclusive. Bars represent +/- 1.5 times the standard error. Event rate and standard error estimates are for interval end. Standard errors are by Greenwood formula.

*Calculated primary patency estimate at 12 months: 79.2% (114/144); KM estimate at 12 months: 92.2%. Subjects event-free at 456 days or later are censored at greater than 456 days. Intervals are end inclusive, e.g. interval 182 is defined as 120-182 days, inclusive. Bars represent +/- 1.5 times the standard error. Event rate and standard error estimates are for interval end. Standard errors are by Greenwood formula.

Duplex ultrasounds were adjudicated by an independent core lab.
Münster Registry

- N=130 (137 lesions)
- 194 mm mean lesion length
- 21% Rutherford 5-6
- 67% PACSS 3/4
- 74% total occlusion
- 61% total lesion coverage

- 46% Diabetes Mellitus
- 19% Chronic Kidney Disease
Primary Patency

- 90% at 2 years
- 71% at 3 years

TLR

- 94% at 2 years
- 80% at 3 years

Clinical Status

Baseline

Rutherford Class (%)

<table>
<thead>
<tr>
<th>Class</th>
<th>Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1-2</td>
<td>0</td>
</tr>
<tr>
<td>Class 3</td>
<td>69</td>
</tr>
<tr>
<td>Class 4</td>
<td>10</td>
</tr>
<tr>
<td>Class 5</td>
<td>16</td>
</tr>
<tr>
<td>Class 6</td>
<td>5</td>
</tr>
</tbody>
</table>

Follow Up

Rutherford Class (%)

<table>
<thead>
<tr>
<th>Class</th>
<th>Follow Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1-2</td>
<td>89</td>
</tr>
<tr>
<td>Class 3</td>
<td>5</td>
</tr>
<tr>
<td>Class 4</td>
<td>0</td>
</tr>
<tr>
<td>Class 5</td>
<td>4</td>
</tr>
<tr>
<td>Class 6</td>
<td>2</td>
</tr>
</tbody>
</table>

Hypoechogenic halo finding in 20%
Prevalence of halo in other studies

- IMPERIAL study 33.7% (1)
- CAPSICUM registry 16.8% (2)
- EMINENT study 26.1% (3)
- Similar findings were described also after use of bare metal stents, stent grafts, Zilver PTX polymer-free drug-coated stents.

Excellent Münster results after two years

....but
what about long-term results?

What is the clinical impact of the hypoechogenic halo findings on the long term performance?
Primary patency at 5 years 65%
Freedom from CD-TLR at 5 years

79%
Cox-regression analysis for primary patency

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>HR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLTI</td>
<td>1.48</td>
<td>0.75 to 2.96</td>
<td>0.261</td>
</tr>
<tr>
<td>CTO</td>
<td>2.20</td>
<td>0.82 to 5.95</td>
<td>0.119</td>
</tr>
<tr>
<td>PACCS 3 or 4</td>
<td>0.75</td>
<td>0.39 to 1.44</td>
<td>0.391</td>
</tr>
<tr>
<td>LL &gt; 250mm</td>
<td>1.5</td>
<td>0.78 to 2.92</td>
<td>0.222</td>
</tr>
<tr>
<td>Stenting over P1</td>
<td>1.28</td>
<td>0.67 to 2.44</td>
<td>0.461</td>
</tr>
<tr>
<td>“Halo” sign</td>
<td>0.24</td>
<td>0.07 to 0.79</td>
<td>0.019</td>
</tr>
</tbody>
</table>

Primary patency at 5 years “halo” + vs “halo” -

P=0.019
Time passage of “halo” to 5 years (n= 27)

- Increased halo diameter n= 2 (7.4 %)
- Decreased halo diameter n=6 (22.2%)
- Unchanged n= 19 (70.4%)
- CD-TLR n= 5 (18.5%)
- Primary patency 87% (vs. 59% for those without halo)
- Mortality (7.4%) 31 and 40 months (unrelated to the stent)
# Eluvia Drug-Eluting Registry summary

<table>
<thead>
<tr>
<th>Primary Patency (KM estimate)</th>
<th>MAJESTIC First in Man</th>
<th>Münster Registry</th>
<th>Auckland All-comers Registry</th>
<th>DESAFINADO</th>
<th>REGAL Registry</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>96.4%</td>
<td>90%</td>
<td>94.0%*</td>
<td>84%</td>
<td>92.2%</td>
</tr>
<tr>
<td>24 months</td>
<td>83.5%</td>
<td>71%</td>
<td>93.8%*</td>
<td>NA</td>
<td>82.9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study design</th>
<th>Single arm, multicentre prospective</th>
<th>Single centre registry</th>
<th>Single centre registry</th>
<th>Single centre registry</th>
<th>Singel arm Multi-centre prospective</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (Eluvia)</td>
<td>57</td>
<td>130</td>
<td>51</td>
<td>64</td>
<td>291</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>70.8 ± 28.1</td>
<td>194 ± 108</td>
<td>105.4</td>
<td>193 ± 128</td>
<td>98.4 ± 73.6</td>
</tr>
<tr>
<td>Occlusion (%)</td>
<td>46%</td>
<td>74%</td>
<td>53%</td>
<td>48%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Results from different trials are not directly comparable. Information provided for educational purposes.


*Observed rate.
Conclusions

• The real-world data are consistent with RCTs results for Eluvia DES despite markedly increased lesion complexity and patient co-morbidities.

• These registries data provide more evidence and more confidence that the Eluvia RCT results are generalizable and repeatable.

• Münster Registry data indicates sustained efficacy and safety of ELUVIA over 5 years of follow-up, similar to IMPERIAL.
Thank you!