“Challenges in diabetic patients: EVOlving PCI’s clinical outcome through innovative technology”

“Session evaluation and key learnings”

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**Disclosure Statement of Financial Interest**

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below. These relationships may lead to bias in my presentation.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>• Grant/Research Support (Institutional)</td>
<td>• None...</td>
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<td>• Advisory Board</td>
<td>• &lt;none</td>
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<td>• Consulting Fees/Honoraria</td>
<td>• Alvimedica</td>
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Diabetes: A global emergency

* IDF Diabetic Atlas 7th Ed. vs 3rd Ed.
** IDF Diabetic Atlas 7th Ed. estimation

- WORLD 246 M (2007)
- WORLD 415 M (2015) +68%*
- WORLD 642 M (2040) +55%**

Legend:
- EUR
- NAC
- WP
- SACA
- SEA
- MENA
- AFR

International Diabetes Federation
Latest polymeric DES have not improved clinical outcome in diabetics

The latest generation DES (embedding permanent or absorbable polymers) has not been able to advance clinical outcome in diabetics. DM patients have always a worst outcome vs. non diabetics.

ZES (Resolute) vs EES (Xience)

Orsiro (Biotronik) vs EES (Xience)
Membrane protein overexpression leads to higher fatty acids bindings/traslocation

Abluminal reservoirs + Amphilimus™ formulation enhance efficacy in diabetics

Abluminal reservoirs, slowly eluting the Amphilimus™ formulation, allow to overcome “-limus” resistance/other hormones proliherative action increasing the uptake of Sirolimus in diabetic cells

**Abluminal RESERVOIRS**

**ARTERIAL WALL**
Drug elution is controlled and directed exclusively towards the vessel wall

**BLOOD FLOW**
Lack of any polymer
Lack of any drug

**AMPHILIMUS™ formulation**

**DIABETIC cell**

Membrane protein overexpression leads to higher fatty acids bindings/traslocation

Membrane Fatty Acid Transporters as Regulators of Lipid Metabolism: Implications for Metabolic Disease - Glatz J; 2010 Physiol Rev 90: 367–417
Cre8™ EVO - New Stent Architecture (EvenArt)

Shortened pitch with reduced crown width and different link number/pattern enhance Elution Profile in challenging anatomies/conditions.
Matched analysis: Cre8 vs. BES
- Diabetic cohort -

Cre8 is STATISTICALLY SUPERIOR to BES:

- TLF = 5% vs. 13% (-62%; p<0.001)
- TLR = 4% vs. 9% (-57%; p=0.005)
Diab8 randomized trial

All-comer patients with diabetes mellitus undergoing PCI

- Cre8™ EVO
- ~3000 patients
- ~55 International Sites
- Randomization 1:1

Everolimus Eluting Stent (EES)

PI: Antonio Colombo

Primary Endpoint

- EFFICACY = 12 months Target Lesion Revascularization (TLR)
  - Sequential check for Non-inferiority (first step) and then for Superiority (second step)

Secondary main Endpoints

- EFFICACY = 24 months TLR for Superiority
- SAFETY = 12 months Cardiac Death + Target Vessel MI (CD + TVMI)

Clinical FU

1 year  2 years  3 years