HOW THE ORSIRO DES PERFORMS IN HIGH-RISK SUBGROUPS

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Speaker's name: Juan F. IGLESIAS

☐ I have no potential conflicts of interest
☑ I have the following potential conflicts of interest to report:

Consultant:

Employment in industry:

Honorarium: Biotronik

Institutional grant/research support:

Owner of a healthcare company:

Stockholder of a healthcare company:
• The management of patients at higher risk of adverse clinical events remains a challenge.

• PCI with durable polymer DES (DP-DES) in high-risk patients has been associated with higher rates of stent failure, including increased risk of ISR, TVR and late/very late ST.

• Biodegradable-polymer DES (BP-DES) have been recently developed to overcome this limitation, with the advantage to potentially:
  – reduce the risk of late adverse clinical events, including very late ST.
  – shorten the duration of DAPT.

• The long-term potential benefit of BP-DES for the management of high-risk subgroups of patients remains undetermined.
CURRENT DRAWBACKS OF DES IN HIGH-RISK PATIENTS
IN-STENT RESTENOSIS

INCIDENCE OF ANGIOGRAPHICALLY DOCUMENTED IN-STENT RESTENOSIS (1998-2009, N=12’904)

### PREDICTORS OF ISR

<table>
<thead>
<tr>
<th>Predictors of restenosis in the overall population</th>
<th>Lower Risk</th>
<th>Higher Risk</th>
<th>OR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st generation DES vs BMS</td>
<td></td>
<td></td>
<td>0.35 [0.31-0.39]</td>
</tr>
<tr>
<td>2nd generation DES vs 1st generation DES</td>
<td></td>
<td></td>
<td>0.67 [0.58-0.77]</td>
</tr>
<tr>
<td>Female gender</td>
<td></td>
<td></td>
<td>0.93 [0.83-1.03]</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td>1.32 [1.19-1.46]</td>
</tr>
<tr>
<td>Multi-vessel disease</td>
<td></td>
<td></td>
<td>1.04 [0.93-1.16]</td>
</tr>
<tr>
<td>History of by-pass surgery</td>
<td></td>
<td></td>
<td>1.38 [1.20-1.58]</td>
</tr>
<tr>
<td>STEMI</td>
<td></td>
<td></td>
<td>1.01 [0.88-1.15]</td>
</tr>
<tr>
<td>NSTEMI</td>
<td></td>
<td></td>
<td>0.97 [0.87-1.08]</td>
</tr>
<tr>
<td>Left main stenting</td>
<td></td>
<td></td>
<td>1.35 [1.02-1.81]</td>
</tr>
<tr>
<td>Left circumflex stenting</td>
<td></td>
<td></td>
<td>1.05 [0.95-1.16]</td>
</tr>
<tr>
<td>Complex lesion</td>
<td></td>
<td></td>
<td>1.35 [1.21-1.51]</td>
</tr>
<tr>
<td>Chronic occlusion</td>
<td></td>
<td></td>
<td>1.21 [1.00-1.48]</td>
</tr>
<tr>
<td>Lesion length (for 10 mm increase)</td>
<td></td>
<td></td>
<td>1.02 [0.96-1.08]</td>
</tr>
<tr>
<td>Vessel size (for 0.5 mm reduction)</td>
<td></td>
<td></td>
<td>1.59 [1.52-1.68]</td>
</tr>
<tr>
<td>Stenosis severity (for 5% DS increase)</td>
<td></td>
<td></td>
<td>1.03 [1.02-1.05]</td>
</tr>
<tr>
<td>Balloon-to-vessel ratio (for 0.1 unit increase)</td>
<td></td>
<td></td>
<td>0.89 [0.85-0.93]</td>
</tr>
<tr>
<td>Maximal balloon pressure (for 1 atm increase)</td>
<td></td>
<td></td>
<td>1.01 [1.00-1.03]</td>
</tr>
<tr>
<td>Stented length (for 10 mm increase)</td>
<td></td>
<td></td>
<td>1.27 [1.21-1.33]</td>
</tr>
</tbody>
</table>

### PROGNOSTIC IMPORTANCE

Adjusted HR: 1.23 (1.03–1.46); P = 0.02
CURRENT DRAWBACKS OF DES IN HIGH-RISK PATIENTS
STENT THROMBOSIS

RATES OF DEFINITE/PROBABLE STENT THROMBOSIS @ 1 YEAR (N= 12’198)

STEMI: INDEPENDENT PREDICTOR OF DEFINITE (HR 3.07, 95% CI 1.32-7.10) AND PROBABLE/DEFINITE (HR 3.36, 95% CI 1.84-6.12) STENT THROMBOSIS

Loh JP, Am J Cardiol. 2014
CURRENT DRAWBACKS OF DES IN STEMI
STENT THROMBOSIS

POTENTIAL MECHANISMS

STEMI
- Increased platelet activation
- Delayed healing at culprit site
- Increased risk of ST

DES implantation
- Lesion complexity
- DAPT cessation
- Stent underexpansion
- Stent malapposition
- Early/late ST

- Chronic inflammatory response elicited by polymer
- Toxic effect of the eluting drug
- Accelerated neo-atherosclerosis
- Impaired vessel healing
- Very late ST

Sarno G, J Am Coll Cardiol. 2014
RECENT DEVELOPMENTS IN DES TECHNOLOGY

OVERVIEW OF NEWER-GENERATION DRUG-ELUTING STENTS DESIGNS

NEW PLATFORM MATERIALS

THINNER STRUTS

THINNER, MORE BIOCOMPATIBLE (DURABLE/BIODEGRADABLE) POLYMERS

NEW ANTIPROLIFERATIVE DRUGS

REDUCED DRUG LOAD

IMPROVED CONTROLLED DRUG RELEASE

IMPROVE BIOCOMPATIBILITY: IMPROVE ARTERIAL HEALING, REDUCE LONG-TERM COMPLICATIONS AND POTENTIALLY REDUCE DAPT DURATION

Stefanini GG, Heart 2014
NOVEL DEVELOPMENTS OF DRUG-ELUTING STENTS
ORSIRO® HYBRID DRUG-ELUTING STENT

UNIQUE HYBRID TECHNOLOGY DESIGNED TO IMPROVE BIOCOMPATIBILITY AND VASCULAR HEALING

Stent platform: PRO-Kinetic Energy
- Cobalt Chromium, L-605
- 60 μm struts, double helix design

Active coating: Biolute
- PLLA* bioabsorbable polymer matrix
- Limus drug (drug load is 1.4 μg/mm²)

Passive coating: proBIO
- Silicon carbide** layer that permanently encapsulates the stent surface, reducing ion release

- ULTRATHIN STRUTS
- BIOCOMPATIBLE POLYMER
- BIOABSORBABLE POLYMER
- THIN POLYMER COATING
- REDUCED DRUG LOAD
- REDUCED THROMBOGENICITY (PLATELET ADHESION)

REDUCE INFLAMMATORY RESPONSE AND IMPROVE ENDOTHELIALIZATION
COMPLEX CORONARY ARTERY DISEASE

ST-ELEVATION MYOCARDIAL INFARCTION (STEMI)
• **DESIGN:**

A prospective, multicenter, international, *non-inferiority*, randomized controlled study.

• **OBJECTIVE:**

To compare Orsiro to Xience Prime stents (2:1 randomization) in *de novo* coronary lesions.

• **PRIMARY ENDPOINT:**

In-stent Late Lumen Loss (LLL) at 9 months.
### BIOFLOW-II
**BASELINE CLINICAL AND LESION CHARACTERISTICS**

<table>
<thead>
<tr>
<th></th>
<th>Orsiro (n=298)</th>
<th>Xience Prime (n=154)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years mean ± SD</strong></td>
<td>62.7 ± 10.4</td>
<td>64.8 ± 9.2</td>
</tr>
<tr>
<td><strong>Gender male (%)</strong></td>
<td>78.2</td>
<td>74.7</td>
</tr>
<tr>
<td><strong>Hypertension (%)</strong></td>
<td>77.5</td>
<td>73.7</td>
</tr>
<tr>
<td><strong>Hyperlipidemia (%)</strong></td>
<td>67.8</td>
<td>73.4</td>
</tr>
<tr>
<td><strong>History of MI (%)</strong></td>
<td>30.2</td>
<td>20.1</td>
</tr>
<tr>
<td><strong>Renal Insufficiency (%)</strong></td>
<td>7.0</td>
<td>4.5</td>
</tr>
<tr>
<td><strong>Congestive Heart Failure (%)</strong></td>
<td>10.1</td>
<td>13.6</td>
</tr>
<tr>
<td><strong>Diabetes (%)</strong></td>
<td>28.2</td>
<td>28.6</td>
</tr>
<tr>
<td><strong>Insulin dependent (%)</strong></td>
<td>21.4</td>
<td>34.1</td>
</tr>
<tr>
<td><strong>Non-insulin dependent (%)</strong></td>
<td>78.6</td>
<td>65.9</td>
</tr>
<tr>
<td><strong>Smoking (%)</strong></td>
<td>66.4</td>
<td>57.8</td>
</tr>
<tr>
<td><strong>History of stroke TIA (%)</strong></td>
<td>7.0</td>
<td>6.5</td>
</tr>
</tbody>
</table>

**MORE COMPLEX TYPE B2 AND C CORONARY ARTERY LESIONS PRESENT IN ONLY 20-30% OF PATIENTS**

Windecker S, Circ Cardiovasc Interv. 2015
BIOFLOW-II: RESULTS
IN-STENT LATE LUMEN LOSS @ 9 MONTHS

P non-inferiority = <0.0001
Difference = 0.00063
95% CI = -0.06 to 0.07

0.10 ± 0.32 mm

0.11 ± 0.29 mm
BIOFLOW-II: LONG-TERM RESULTS
TARGET LESION FAILURE @ 36 MONTHS

Target Lesion Failure Composites (%)

- Cardiac Death: Orsiro 0.7, Xience Prime 1.3, P = 0.5069
- Target vessel MI: Orsiro 3.4, Xience Prime 2.6, P = 0.6590
- TLR (Clinically driven): Orsiro 5.6, Xience Prime 6.7, P = 0.6361
- CABG (Emergent): Orsiro 0.0, Xience Prime 0.0, P > 0.9999

Days after PCI: 0, 180, 365, 730, 1095

Graph showing TLF universal def. (%): Orsiro 9.0%, Xience Prime 10.6%, P = 0.5800
BIOFLOW-II: RESULTS IN HIGH-RISK SUBGROUPS
TARGET LESION FAILURE @ 36 MONTHS

DIABETICS

Target Lesion Failure Composites (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Orsiro N=84</th>
<th>Xience N=44</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Death</td>
<td>0.0</td>
<td>2.3</td>
<td>0.3437</td>
</tr>
<tr>
<td>Target vessel MI</td>
<td>1.2</td>
<td>0.0</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>TLR (Clinically driven)</td>
<td>11.1</td>
<td>6.9</td>
<td>0.4688</td>
</tr>
<tr>
<td>CABG (Emergent)</td>
<td>0.0</td>
<td>0.0</td>
<td>&gt;0.9999</td>
</tr>
</tbody>
</table>

P value = 0.6021

BIOFLOW- II: RESULTS IN HIGH-RISK SUBGROUPS
TARGET LESION FAILURE @ 36 MONTHS

SLAGBOOM et al. Poster EuroPCR 2015, Paris, France
BIOFLOW-II: RESULTS IN HIGH-RISK SUBGROUPS
TARGET LESION FAILURE @ 36 MONTHS

SMALL VESSELS

TLF univ. def. (%)

Orsiro
Xience Prime

Cardiac Death
0.0
1.1
0.3514

Target vessel MI
3.7
4.4
0.7475

TLR (Clinically driven)
8.1
8.9
0.8249

CABG (Emergent)
0.0
0.0
>0.9999

P=0.3494

BIOFLOW-II - II: RESULTS IN HIGH-RISK SUBGROUPS
TARGET LESION FAILURE @ 36 MONTHS

Slagboom et al. Poster EuroPCR 2015, Paris, France
• **NO DEFINITIVE STENT THROMBOSIS @ 36 MONTHS IN BOTH TREATMENT ARMS.**

• **ONLY ONE DIABETIC PATIENT IN THE XIENCE PRIME ARM EXPERIENCED A VERY LATE POSSIBLE STENT THROMBOSIS.**

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**BIOFLOW-II: LONG-TERM RESULTS**

**STENT THROMBOSIS @ 36 MONTHS**

**All Subjects**

- Xience Prime: 0.7%
- Orsiro: 0.0%
- Days after PCI: 0, 180, 365, 730, 1095
- **P=0.3407**

**Diabetics**

- Xience Prime: 2.3%
- Orsiro: 0.0%
- Days after PCI: 0, 180, 365, 730, 1095
- **P=0.3437**

**Small Vessel**

- Xience Prime: 0.0%
- Days after PCI: 0, 180, 365, 730, 1095
- **P>0.9999**

Slagboom et al. Poster EuroPCR 2015, Paris, France
• DESIGN:
   International, prospective, non-randomized, multicenter and open-label clinical evaluation.

• OBJECTIVE:
   To assess the clinical performance of the ORSIRO DES in coronary arteries in an “all comers” population.

• PRIMARY ENDPOINT:
   Target lesion failure (TLF, composite of cardiac death, target vessel MI, CABG and clinically-driven TLR) at 12 months.
### BIOFLOW-III

#### BASELINE CLINICAL AND LESION CHARACTERISTICS

<table>
<thead>
<tr>
<th>Patients</th>
<th>N = 1’356</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>66 ± 11 yrs</td>
</tr>
<tr>
<td>Male % (N)</td>
<td>72% (971)</td>
</tr>
<tr>
<td>Age ≥ 75 yrs</td>
<td>25% (335)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>76% (1,029)</td>
</tr>
<tr>
<td>Hypercholesteremia</td>
<td>60% (815)</td>
</tr>
<tr>
<td>Smoking</td>
<td>55% (741)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>30% (403)</td>
</tr>
<tr>
<td>Insulin dependent</td>
<td>34% (138)</td>
</tr>
<tr>
<td>Non-Insulin dependent</td>
<td>66% (256)</td>
</tr>
<tr>
<td>History of MI</td>
<td>28% (376)</td>
</tr>
<tr>
<td>Acute MI</td>
<td>33% (442)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesion</th>
<th>N = 1,738</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small vessels (≤2.75mm)</td>
<td>48% (828)*</td>
</tr>
<tr>
<td>Chronic Total Occlusion</td>
<td>4% (65)</td>
</tr>
</tbody>
</table>

*Related to 1,724 lesions

**ACC/AHA LESION CLASSIFICATION**

- A 12%
- B1 36%
- B2 32%
- C 20%

**MORE COMPLEX TYPE B2 AND C CORONARY ARTERY LESIONS PRESENT IN 50% OF PATIENTS**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mm ± SD)</td>
<td>15.8 ± 9.1</td>
</tr>
<tr>
<td>Ref. vessel diameter (mm ± SD)</td>
<td>3.0 ± 0.4</td>
</tr>
<tr>
<td>Diameter stenosis (% ± SD)</td>
<td>85.6 ± 13.4</td>
</tr>
<tr>
<td>Moderate calcification</td>
<td>24%</td>
</tr>
<tr>
<td>Severe calcification</td>
<td>7%</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>16%</td>
</tr>
</tbody>
</table>

Waltenberger J, Eurointervention 2015
BIOFLOW-III: RESULTS

TARGET LESION FAILURE (TLF) @ 12 MONTHS

LOW TLF AND ST RATES IN AN UNSELECTED, ALL-COMERS POPULATION WITH COMPLEX CORONARY ARTERY DISEASE
COMPLEX CORONARY ARTERY DISEASE

ST-ELEVATION MYOCARDIAL INFARCTION (STEMI)
VASCULAR RESPONSE IN STEMI
IMPACT OF UNDERLYING LESION CHARACTERISTICS

DIFFERENT LESION MORPHOLOGICAL AND PATHOLOGICAL CHARACTERISTICS

STABLE CORONARY ARTERY DISEASE

FIBROATHEROMA WITH THICK FIBROUS CAP

CULPRIT SITE IN ACUTE STEMI vs. STABLE CAD LESIONS

- LARGER LIPID-LADEN NECROTIC CORE
- PENETRATION OF THE NECROTIC CORE BY STENT STRUTS
- THINNER FIBROUS CAP
- PRESENCE OF THROMBUS
- REDUCED NEO-INTIMAL THICKNESS

ACUTE STEMI: DELAYED ARTERIAL HEALING, AND INCREASED RISK OF STENT THROMBOSIS

ACUTE STEMI

- REDUCED NEO-INTIMAL THICKNESS
- INCREASED PERCENTAGE OF UNCOVERED STRUTS
- INCREASED PERCENTAGE OF STRUTS WITH INFLAMMATION
- INCREASED PERCENTAGE OF STRUTS WITH FIBRIN

Nakazawa G, Circulation 2008
VASCULAR RESPONSE IN STEMI
EARLY-GENERATION DP-DES

DELAYED ARTERIAL HEALING AND INCREASED RISK OF STENT THROMBOSIS AFTER PCI WITH DES FOR STEMI

S UDDEN DEATH 9 MONTHS AFTER PES FOR STEMI

POSSIBLE EXPLANATIONS

• HIGH AFFINITY OF HIGHLY LIPOPHILIC DRUGS FOR LIPID-RICH PLAQUES (PENETRATION OF THE STENT STRUTS INTO THE NECROTIC CORE).

• REDUCED COVERAGE OF LIPID-RICH NECROTIC CORE (AVASCULAR) BY MIGRATING AND PROLIFERATING CELLS.

• ABSENCE OR REDUCED NUMBER OF SMOOTH MUSCLE CELLS IN RUPTURED FIBROUS CAPS.

• DELAYED SMOOTH MUSCLE CELL PROLIFERATION AND ENDOTHELIAL REGROWTH WITH HIGHER DRUG CONCENTRATIONS.

• INCREASED DRUG UPTAKE BY THROMBUS (Hwang CW, Circulation 2005).

Nakazawa G, Circulation 2008
VASCULAR RESPONSE IN STEMI
NEWER-GENERATION DP-DES

NEWER-GENERATION DP-DES ARE STILL ASSOCIATED WITH
PERSISTENT INFLAMMATORY REACTION, NEOATHEROSCLEROSIS AND RISK OF THROMBOSIS

CoCr EES
Focal inflammation
Focal inflammation with eosinophils (4 months)

CoNi ZES
Chronic Inflammation
Chronic inflammation with giant cells secondary to polymer delamination (3 months)

CoCr EES
Neoatherosclerosis
Foamy macrophage accumulation (neoatherosclerosis)

CoCr EES
Late Stent Thrombosis
EES implanted within PES 6 months antemortem

TRANSLATION INTO CLINICAL TRIALS WITH HARD CLINICAL ENDPOINTS IN STEMI?
Otsuka F, Circulation 2014
NEWER-GENERATION DES vs. BMS IN STEMI @ 1 YEAR

POOLED ANALYSIS OF COMFORTABLE-AMI AND EXAMINATION TRIALS (N= 2’665)

**TARGET LESION REVASCULARIZATION**

- Meta-analyses HR, 0.32 (95% CI, 0.20-0.52)
  - P<0.001

**DEFINITE/PROBABLE STENT THROMBOSIS**

- Meta-analyses HR, 0.53 (95% CI, 0.29-0.95)
  - P=0.033

** IMPROVED SHORT-TERM EFFICACY **

** IMPROVED SHORT-TERM SAFETY **
EARLY- vs. NEWER-GENERATION DP-DES IN STEMI @ 3 YEARS RACES-MI TRIAL

TARGET VESSEL REVASCULARIZATION

DEFINITE/PROBABLE STENT THROMBOSIS

PRESERVED LONG-TERM EFFICACY

IMPROVED LONG-TERM SAFETY

Di Lorenzo E, J Am Coll Cardiol Intv 2014
EARLY- vs. NEWER-GENERATION DP-DES IN STEMI @ 3 YEARS
XAMI TRIAL

DURABLE-POLYMER EES vs. DURABLE POLYMER SES @ 3 YEARS (N=625)

CARDIAC DEATH, MI, TVR

DEFINITE/PROBABLE STENT THROMBOSIS

PRESERVED LONG-TERM EFFICACY

TREND TOWARDS IMPROVED LONG-TERM SAFETY

Hofma SH, Eurointervention 2015
META-ANALYSIS, 28 RCTs, 34’068 PATIENT-YEARS OF FOLLOW-UP

TARGET LESION REVASCULARIZATION

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
<th>Treatment</th>
<th>Control</th>
<th>Rate Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.46</td>
<td>0.38</td>
</tr>
<tr>
<td>PES vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.69</td>
<td>0.53</td>
</tr>
<tr>
<td>EES vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.42</td>
<td>0.26</td>
</tr>
<tr>
<td>ZES vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.96</td>
<td>0.43</td>
</tr>
<tr>
<td>ZES-R vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.26</td>
<td>0.04</td>
</tr>
</tbody>
</table>

PROBABLE/DEFINITE STENT THROMBOSIS

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
<th>Treatment</th>
<th>Control</th>
<th>Rate Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.94</td>
<td>0.69</td>
</tr>
<tr>
<td>PES vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>1.11</td>
<td>0.75</td>
</tr>
<tr>
<td>EES vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.39</td>
<td>0.18</td>
</tr>
<tr>
<td>ZES vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.69</td>
<td>0.23</td>
</tr>
<tr>
<td>ZES-R vs. BMS</td>
<td></td>
<td></td>
<td></td>
<td>0.62</td>
<td>0.10</td>
</tr>
</tbody>
</table>

NO SIGNIFICANT DIFFERENCE BETWEEN FIRST- AND SECOND-GENERATION DES WITH DURABLE POLYMER (EES/ZES/ZES-R) IN TERMS OF CLINICAL EFFICACY IN PATIENTS WITH STEMI

WHAT ABOUT NEWER-GENERATION DES WITH BIODEGRADABLE POLYMER IN STEMI?
BP-DES vs. DP-DES
LEADERS TRIAL: STEMI SUBGROUP ANALYSIS

BIODEGRADABLE-POLYMER BES vs. DURABLE-POLYMER SES @ 5 YEARS (N=275)

CARDIAC DEATH, MI, CLINICALLY-INDICATED TVR

PROBABLE/DEFINITE STENT THROMBOSIS

STRONG SIGNAL TOWARDS A SIGNIFICANT REDUCTION OF MACE IN PATIENTS WITH STEMI

IMPROVED LONG-TERM EFFICACY

TREND TOWARDS IMPROVED LONG-TERM SAFETY

Zhang YJ, Heart 2015
BP-DES vs. DP-DES IN STEMI

POOLED ANALYSIS FROM ISAR-TEST 3, ISAR-TEST 4 AND LEADERS TRIALS (N= 497)
BIODEGRADABLE POLYMER DES vs. EARLY GENERATION DURABLE POLYMER SES @ 4 years

TARGET LESION REVASCULARIZATION

RRR 46%
ARR 5.7%

HR 0.54 (95% CI: 0.30-0.98)
p=0.04

Permanent polymer 13.1%
Biodegradable polymer 7.4%

PROBABLE/DEFINITE STENT THROMBOSIS

RRR 51%
ARR 3.5%

HR 0.49 (95% CI: 0.22-1.11)
p=0.09

Permanent polymer 7.1%
Biodegradable polymer 3.6%

IMPROVED LONG-TERM EFFICACY

IMPROVED LONG-TERM SAFETY
### Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>STEMI N = 144</th>
<th>NSTEMI N = 293</th>
<th>All Other N = 437</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>61.5 ± 11.0</td>
<td>66.7 ± 11.8</td>
<td>66.7 ± 10.2</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>57.6% (83)</td>
<td>71.0% (208)</td>
<td>80.3% (738)</td>
</tr>
<tr>
<td>Hypercholesteremia*</td>
<td>45.8% (66)</td>
<td>52.6% (154)</td>
<td>64.7% (595)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23.6% (34)</td>
<td>27.0% (79)</td>
<td>31.4% (289)</td>
</tr>
</tbody>
</table>

### Lesion Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>STEMI N = 144</th>
<th>NSTEMI N = 293</th>
<th>All others N = 919</th>
</tr>
</thead>
<tbody>
<tr>
<td>B2/C type lesions</td>
<td>66.3% (110)</td>
<td>54.0% (204)</td>
<td>49.5% (591)</td>
</tr>
<tr>
<td>Mean stent length (mm)</td>
<td>18.6 ± 5.5</td>
<td>17.8 ± 5.8</td>
<td>18.2 ± 5.8</td>
</tr>
<tr>
<td>Mean stent diameter (mm)</td>
<td>3.1 ± 0.4</td>
<td>3.0 ± 0.4</td>
<td>3.0 ± 0.4</td>
</tr>
</tbody>
</table>

### Target Lesion Failure (TLF) @ 12 Months

<table>
<thead>
<tr>
<th>Event</th>
<th>STEMI</th>
<th>NSTEMI</th>
<th>All Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Death</td>
<td>8.3%</td>
<td>5.0%</td>
<td>3.6%</td>
</tr>
<tr>
<td>MI</td>
<td>2.1%</td>
<td>2.1%</td>
<td>1.9%</td>
</tr>
<tr>
<td>TLR</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2’119 Patients with stable CAD or ACS undergoing PCI

INCLUSION CRITERIA

• Age ≥ 18 years
• Stable coronary artery disease, silent ischemia, acute coronary syndromes: UA, NSTEMI, and STEMI
• At least one lesion with diameter stenosis >50% in a native coronary artery or a bypass graft
• No limitation regarding the number of vessels or lesions and lesion length

EXCLUSION CRITERIA

• Pregnancy
• Planned surgery within 6 months of PCI
• Intolerance to aspirin, clopidogrel, heparin, sirolimus, everolimus, contrast material
• Inability to provide informed consent
• Participation in another trial

Pilgrim T, Am Heart J 2014
BIOSCIENCE: LONG-TERM RESULTS
TARGET LESION FAILURE (TLF) @ 24 MONTHS

RR (95%CI)=1.00 (0.77-1.31)
P= 0.98

Number at risk
- DP-EES: 1056 1007 1001 996 988 975 965 940 935 929 924 917 907
- BP-SES: 1063 1012 1002 989 975 967 958 935 928 918 911 908 889

Definite ST

Definite/probable ST

BP SES

DP EES

2,119 patients included

407 STEMI patients

Rx stratified according to presence or absence of STEMI

211 allocated to biodegradable polymer sirolimus-eluting stent
   (289 lesions)

204 follow-up information for primary endpoint available

211 analysed for clinical endpoint
   - 7 censored at timepoint of refusal or loss to follow-up

196 allocated to durable polymer everolimus-eluting stent
   (267 lesions)

191 follow-up information for primary endpoint available

196 analysed for clinical endpoint
   - 5 censored at timepoint of refusal or loss to follow-up

STRONG SIGNAL TOWARDS A SIGNIFICANT REDUCTION IN TLF IN THE PRESPECIFIED SUBGROUP OF PATIENTS WITH STEMI
Despite little available data, the Orsiro Hybrid DES demonstrates a comparable clinical performance to the current state-of-the-art new-generation DP-DES in patients at high-risk of adverse events, with low TLF and stent thrombosis rates, similar to rates in the low-risk subgroups.

Recent data with newer-generation BP-DES demonstrate a CONSISTENT and STRONG SIGNAL towards a SIGNIFICANT REDUCTION IN MACE among patients with STEMI, compared with both early- (LEADERS) and newer-generation (BIOSCIENCE) DP-DES.

These data strongly suggest that new-generation BP-DES with enhanced biocompatibility, like the Orsiro Hybrid DES, may have a particular clinical benefit in a high-risk subgroup of patients but warrants confirmation in appropriately designed randomized controlled trials.
THANK YOU FOR YOUR ATTENTION