ISAR-LEFT MAIN 2
Randomized Trial

Zotarolimus- vs. Everolimus-Eluting Stents for Treatment of Unprotected Left Main Coronary Artery Lesions

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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.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Lecture fees</td>
<td>Abbott Vascular</td>
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<td>Daichii Sankyo/Lilly</td>
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<td>The Medicines</td>
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PCI vs. CABG Surgery for uLMCA

Meta-analysis of Randomized Controlled Studies

Similar Risk of Death or Myocardial Infarction

Higher Risk of Revascularization

Capodanno et al., J Am Coll Cardiol 2011
First Generation DES for uLMCA
Similar Clinical & Angiographic Performance

Death, Myocardial Infarction or Reintervention

RR 0.99 (95% CI, 0.69-1.42), P=.96

<table>
<thead>
<tr>
<th>Patients at Risk</th>
<th>Years after randomization</th>
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<tr>
<td></td>
<td>0</td>
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<tr>
<td>PES</td>
<td>302</td>
</tr>
<tr>
<td>SES</td>
<td>305</td>
</tr>
<tr>
<td></td>
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<td>SES</td>
<td>271</td>
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<td>PES</td>
<td>250</td>
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<tr>
<td>SES</td>
<td>252</td>
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</table>

Mehilli et al., J Am Coll Cardiol 2009
Second Generation DES for All-Comers

Resolute All Comers trial

Serruys et al., New Engl J Med 2010
ISAR-LEFT MAIN 2

DESIGN:
Randomized, multi-center trial

OBJECTIVE:
To evaluate the relative performance of two 2nd generations DES – zotarolimus- and everolimus-eluting stents – in patients with uLMCA lesions

STEERING COMMITTEE
Adnan Kastrati, MD (Chair)
Julinda Mehilli, MD (principal investigator)
Josef Dirschinger, MD

PARTICIPATING CENTERS
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Bad Segeberger Kliniken, Bad Segeberg, Germany
   PI: G Richart
Department of Cardiology, University of Ferrara, Italy
   PI: M Valgimigli
Endpoints

**Primary endpoint:**
Incidence of major adverse cardiac events defined as the composite of death, myocardial infarction, target lesion revascularization at 1-year follow-up

**Secondary endpoints:**
Incidence of definite/probable stent thrombosis at 1-year follow-up
Angiographic restenosis at 6-9-month follow-up

**Study hypothesis:**
Endeavor Resolute stent is not inferior to Xience stent in terms of major adverse cardiac events
ISAR-LEFT MAIN 2 Trial

650 patients with uLMCA lesions
pre-treated with 600 mg clopidogrel

Zotarolimus-eluting stent
(Endeavor Resolute)
N= 324

Angiographic follow-up
at 8 months in 73%
(N=237)

Clinical follow-up at
12 months in 100%
(N=324)

Everolimus-eluting stent
(Xience)
N= 326

Angiographic follow-up
at 8 months in 69%
(N=226)

Clinical follow-up at
12 months in 100%
(N=326)
Sample Size Calculation

**Hypothesis:**
Endeavor Resolute stent is not inferior to Xience stent in terms of major adverse cardiac events

**Assumptions:**
- Incidence of MACE 25% in both stent groups
- Margin of non-inferiority 9%
- Power of 80%
- \( \alpha \)-level of 0.05
- Rate of lost to follow-up 5%

Planned number of patients for each group: 300
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Resolute</th>
<th>Xience</th>
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<tbody>
<tr>
<td></td>
<td>n=324</td>
<td>n=326</td>
</tr>
<tr>
<td>Age, years</td>
<td>69.4±10.4</td>
<td>70.2±9.4</td>
</tr>
<tr>
<td>Women, %</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td>ACS, %</td>
<td>38</td>
<td>33</td>
</tr>
<tr>
<td>History of MI, %</td>
<td>32</td>
<td>29</td>
</tr>
<tr>
<td>Malignancies, %</td>
<td>22</td>
<td>24</td>
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<tr>
<td>Parsonnet Score</td>
<td>13.3±10.3</td>
<td>13.7±11.0</td>
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## Angiographic and Procedural Characteristics

<table>
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<tr>
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<th>Resolute n=324</th>
<th>Xience n=326</th>
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<tbody>
<tr>
<td>Multivessel CAD, %</td>
<td>69</td>
<td>74</td>
</tr>
<tr>
<td>Distal lesion location, %</td>
<td>83</td>
<td>77</td>
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<tr>
<td>Single stenting technique, %</td>
<td>62</td>
<td>66</td>
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</tbody>
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Major Adverse Cardiac Events
- primary endpoint -

RR 1.26 (95% CI 0.85-1.85)
$P = .25$

Resolute 17.5%
Xience 14.3%

Mortality 5.6% both
Incidence of Stent Thrombosis
- secondary endpoint -

Resolute
n=324

Probable stent thrombosis
Definite stent thrombosis

Xience
n=326

0.6
0.3
0.6
0.0

TCT2012
<table>
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<tr>
<th></th>
<th>Angiographic restenosis</th>
<th>Clinical restenosis</th>
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<tbody>
<tr>
<td>P value</td>
<td>P = .20</td>
<td>P = .35</td>
</tr>
<tr>
<td>LMCA Area Restenosis</td>
<td>21.5%</td>
<td>11.7%</td>
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**Resolute**

**Xience**
The use of 2\textsuperscript{nd} gen. DES in unprotected LMCA lesions in relatively unselected patients is feasible, safe and effective.

Both Endeavor Resolute and Xience stents provide similar clinical and angiographic outcomes at one-year follow-up in this high risk patient population.
Background

Patients undergoing invasive treatment of unprotected left main coronary artery (uLMCA) lesions are considered at high-risk of adverse cardiovascular events.

The use of 1st generation drug-eluting stents in these lesions has been shown feasible, safe and effective. The zotarolimus-eluting, Endeavor Resolute stent and everolimus-eluting, Xience stent both second generation drug-eluting stents perform very similar in nearly all coronary artery lesions.

However, their performance in uLMCA lesions has not been assessed.