ISAR-LEFT MAIN: A Randomized Clinical Trial on Drug-Eluting Stents for Unprotected Left Main Lesions

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Although CABG surgery and BMS for unprotected LM disease demonstrate similar mortality rates, the higher incidence of restenosis and greater need for revascularization attenuate the clinical efficacy of LM stenting.

DES may be particularly helpful to reduce restenosis in the high risk subset of pts with LM disease. Importantly, for pts who are unable to undergo CABG surgery, DES remain the only revascularization alternative.
Two DES (Cypher and Taxus) are highly but probably not equally effective in reducing restenosis.

Patients with LM lesions deserve the best DES. In particular, we need to know which is the best DES to use in head-to-head comparisons of DES versus CABG in patients with LM lesions.
Objective of ISAR-LEFT MAIN

…to assess the relative efficacy of the sirolimus-eluting stent (Cypher) and paclitaxel-eluting stent (Taxus) in patients with unprotected LM lesions.
Patients with ischemic symptoms or evidence of myocardial ischemia in the presence of ≥50% stenosis located in unprotected LM lesions who are unable to undergo CABG (poor surgical candidates or unwillingness).

Informed, written consent
Exclusion Criteria

Age < 18 years
Cardiogenic shock
ST-Elevation Acute Myocardial Infarction
In-stent Restenosis
Prior coronary artery bypass surgery
Left main size > 4.5 mm by visual estimation
Malignancies with life expectancy < 1 year
Planned staged PCI within 30 days from index PCI
Planned elective surgical procedure necessitating discontinuation of clopidogrel during the first 6 months
Pregnancy
Incidence of major adverse cardiac events defined as the composite of death, myocardial infarction and target lesion revascularization at 1-year follow-up.
Angiographic restenosis at 6-9-month FU angiogram, defined as diameter stenosis $\geq 50\%$ measured by QCA in the area from left main ostium to 5-mm proximal segments of LAD, LCx as well as of R. intermedius if the latter has a reference diameter $>2$ mm.
Sample size calculation

Hypothesis:
Taxus is not inferior to Cypher in terms of major adverse cardiac events

Assumptions:
Incidence of MACE 25% in the Cypher group
Margin of non-inferiority 9%
Power of 80%
$\alpha$-level of 0.05

Needed number of patients for each group: 287
Planned number of patients to enroll: 600 in total
Intracoronary Stenting and Angiographic Results:
Drug-Eluting Stents for Unprotected Coronary Left Main Lesions

607 patients with unprotected left main lesions
Clopidogrel 600 mg at least 2h before procedure
Aspirin 500mg i.v.

Sirolimus-eluting stent (Cypher)  
n=305

Paclitaxel-eluting stent (Taxus)  
n=302

Clopidogrel 2x75 mg/day until discharge
75 mg indefinitely
Aspirin 200 mg/day
Follow-Up Protocol

600 mg Clopidogrel
PCI
ASS 500 mg + heparin with/out GPI (10%) or bivalirudin (15%)

0 30 d 6-8 mo. 12 mo.

↑↑↑
serial CK + CKMB measurements
clinical follow-up (100%)

↑
clinical follow-up

↑
repeat angiography
## Baseline clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Cypher n=305</th>
<th>Taxus n=302</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>69.4±9.3</td>
<td>68.8±10.3</td>
</tr>
<tr>
<td>Women, %</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>Art. Hypertension, %</td>
<td>69</td>
<td>70</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>75</td>
<td>78</td>
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</table>
### Baseline clinical characteristics (con’t)

<table>
<thead>
<tr>
<th></th>
<th>Cypher n=305</th>
<th>Taxus n=302</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstable Angina, %</td>
<td>23</td>
<td>27</td>
</tr>
<tr>
<td>Non-ST-elevation AMI, %</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>History of MI, %</td>
<td>28</td>
<td>25</td>
</tr>
<tr>
<td>Prior PCI, %</td>
<td>50</td>
<td>46</td>
</tr>
<tr>
<td>Parsonnet Score</td>
<td>12.0±9.1</td>
<td>12.8±9.8</td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>4.4±3.2</td>
<td>4.7±3.5</td>
</tr>
<tr>
<td>IABP, %</td>
<td>1</td>
<td>1</td>
</tr>
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</table>
## Angiographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Cypher n=305</th>
<th>Taxus n=302</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV ejection fraction, %</td>
<td>54.4±12.4</td>
<td>53.4±12.8</td>
</tr>
<tr>
<td>Coronary artery dominance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>right</td>
<td>80</td>
<td>78</td>
</tr>
<tr>
<td>left</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>balanced</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>RCA ≥50% stenosis, %</td>
<td>74</td>
<td>71</td>
</tr>
<tr>
<td>Dominant RCA occlusion, %</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>R. intermedius &gt;2.0 mm, %</td>
<td>24</td>
<td>25</td>
</tr>
</tbody>
</table>
Left main lesion location

<table>
<thead>
<tr>
<th>Location</th>
<th>Cypher n=305</th>
<th>Taxus n=302</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ostial</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Body</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>Ostial + body</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>43</td>
<td>41</td>
</tr>
<tr>
<td>Trifurcation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>
Stent techniques:

- Single stenting
- Culotte stenting
- T-stenting
- Trifurcation stenting

Cypher:
- Trifurcation stenting: 1
- T-stenting: 46
- Culotte stenting: 51
- Single stenting: 51
  - Total: 305

Taxus:
- Trifurcation stenting: 1
- T-stenting: 41
- Culotte stenting: 57
- Single stenting: 57
  - Total: 302
Incidence of Stent Thrombosis
- ARC Definition -

Cypher
n=305

Definite stent thrombosis
Probable stent thrombosis

Taxus
n=302

Probable stent thrombosis
Definite stent thrombosis

0.7
0.3
0.3
0.0

%
Death or Myocardial Infarction

Days after randomization

% over Time

Cypher
Taxus
Composite of Death, MI or Reintervention

Days after randomization

Cypher
Taxus
This trial, the largest LM randomized trial to date, shows that unprotected LM stenting with Cypher or Taxus is feasible and safe at short-term.

Cypher and Taxus stents provide comparable short-term safety.

One-year outcomes (primary endpoint of the trial) will better clarify whether there are differences between these devices.