Trial of Everolimus-Eluting Stents or Bypass Surgery for Coronary Disease (BEST Trial)

Seung-Jung Park, MD, PhD
On behalf of the BEST investigators

Professor of Medicine, University of Ulsan College of Medicine, Heart Institute, Asan Medical Center, Seoul, Korea
Recent studies have demonstrated that the rates of most adverse clinical outcomes in patients with multivessel coronary-artery disease are lower following CABG than with PCI.

However, previous studies may have been limited by their use of first-generation drug-eluting stents. Although these stents reduced the rate of restenosis, their use was associated with a relatively high rate of stent-related thrombotic events.
### BEST Trial

#### Design

- **DESIGN:** a prospective, open-label, randomized trial

- **OBJECTIVE:** To compare PCI with everolimus-eluting stents and CABG for optimal revascularization of patients with multivessel coronary artery stenosis.

- **PRINCIPAL INVESTIGATOR**
  Seung-Jung Park, MD, PhD, Asan Medical Center, Seoul, Korea
<table>
<thead>
<tr>
<th>Country</th>
<th>Site</th>
<th>Investigator</th>
</tr>
</thead>
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<td>Korea</td>
<td>Asn Medical center</td>
<td>Seung-Jung Park</td>
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<td>Seung Ho Hur</td>
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<td>Sang-Gon Lee</td>
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<tr>
<td>Malaysia</td>
<td>National Heart Institute</td>
<td>Robaaya Zambahari</td>
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</tbody>
</table>
Major Inclusion Criteria

- ≥ 18 years of age.
- Angiographically confirmed multivessel coronary artery disease (>70%)
- Suitable candidates for either PCI or CABG by their treating physicians and surgeons
- Symptoms of angina and/or objective evidence of myocardial ischemia.
Major Exclusion Criteria

- Any contraindication to dual antiplatelet therapy
- Severe heart failure (NYHA III or IV)
- Planned surgery
- Previous CABG
- Prior PCI with DES implantation within 1 year
- CTO ≥2
- STEMI within 72 hours
- Elevated cardiac enzyme
- Disabled stroke
- Other comorbidity
Study Procedures

- **Everolimus-Eeluting Xience Stent** for all lesions
- Strong recommendation of IVUS-guidance
- Other adjunctive devices at the physician’s discretion
- Use of LIMA to LAD anastomosis
- Off- or on-pump surgery at the surgeon’s discretion
- DAPT at least for 1 year after PCI
- Standard medical treatment after PCI and CABG
Follow-up

- Clinical follow-up at 30 days and 6, 9, and 12 months, and annually thereafter, via clinic visit or telephone interview.
- Secondary preventive medication was strongly recommended according to clinical guideline.
- Routine angiographic follow-up was strongly discouraged for all patients to reduce the occurrence of repeat revascularization driven by angiography alone without signs or symptoms of ischemia.
Primary End Point

- A composite of major adverse cardiac events (MACE) for the 2 years after randomization including
  - Death from any cause
  - Myocardial infarction
  - Target vessel revascularization
Original Power Calculation

Non-inferiority Design for Primary Endpoint

- Assumed MACE rate: 12% at 2 years
- A noninferiority margin: 4%
- A one-sided type I error rate: 0.05
- Power: 80%
- Dropout rate: 5%
- Assumed sample size: 1776 patients
Premature Termination of Trial

- The enrollment rate was slower than expected, which was thought to be a consequence of the rapid spread of measurement of fractional flow reserve in clinical practice.
- The data and safety monitoring board recommended stopping enrollment in October 2013 when 880 patients had been enrolled.
- We extended the follow-up period with a median of 4.6 years.
Patient Flow

4654 patients were screened

1725 patients were eligible

880 patients consented and enrolled
Between July 2008 and September 2013

438 patients assigned to PCI
Treated CABG: 19
Treated PCI: 413
Treated medically: 6

1 Year FU (N=438)
3 Year FU (N=369)
5 Year FU (N=172)

442 patients assigned to CABG
Treated CABG: 382
Treated PCI: 51
Treated medically: 9

1 Year FU (N=438)
3 Year FU (N=369)
5 Year FU (N=172)
Kaplan-Meier method to estimate survivals with comparison using log-rank test.
Noninferiority test using the Z-test with 95% CI of difference in the 2-year MACE rate.
Survival analyses using longer-term outcomes using all available follow-up data as an exploratory analyses.
Subgroups analysis using the Cox regression model with tests for interaction.
Primary analysis in intention-to-treat principle
## Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>PCI (N=438)</th>
<th>CABG (N=442)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>64.0 ± 9.3</td>
<td>64.9 ± 9.4</td>
<td>0.13</td>
</tr>
<tr>
<td>Male sex</td>
<td>304 (69.4)</td>
<td>325 (73.5)</td>
<td>0.18</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.7 ± 2.9</td>
<td>2.0 ± 2.9</td>
<td>0.16</td>
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<tr>
<td>Diabetes</td>
<td>177 (40.4)</td>
<td>186 (42.1)</td>
<td>0.62</td>
</tr>
<tr>
<td>Hypertension</td>
<td>296 (67.6)</td>
<td>295 (66.7)</td>
<td>0.79</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>239 (54.6)</td>
<td>222 (50.2)</td>
<td>0.20</td>
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<tr>
<td>Current smoker</td>
<td>88 (20.1)</td>
<td>89 (20.1)</td>
<td>0.99</td>
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<tr>
<td>Previous PCI</td>
<td>30 (6.8)</td>
<td>38 (8.6)</td>
<td>0.33</td>
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<tr>
<td>Previous myocardial infarction</td>
<td>25 (5.7)</td>
<td>29 (6.6)</td>
<td>0.60</td>
</tr>
<tr>
<td>Previous congestive heart failure</td>
<td>16 (3.7)</td>
<td>12 (2.7)</td>
<td>0.43</td>
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</tbody>
</table>
## Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PCI (N=438)</th>
<th>CABG (N=442)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic renal failure</td>
<td>9 (2.1)</td>
<td>7 (1.6)</td>
<td>0.60</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>15 (3.4)</td>
<td>12 (2.7)</td>
<td>0.54</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>8 (1.8)</td>
<td>6 (1.4)</td>
<td>0.58</td>
</tr>
<tr>
<td>Clinical manifestation</td>
<td></td>
<td></td>
<td>0.68</td>
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<tr>
<td>Stable angina or asymptomatic</td>
<td>210 (47.9)</td>
<td>204 (46.2)</td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td>185 (42.2)</td>
<td>199 (45.0)</td>
<td></td>
</tr>
<tr>
<td>Recent acute myocardial infarction</td>
<td>43 (9.8)</td>
<td>39 (8.8)</td>
<td></td>
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<tr>
<td>Ejection fraction, %</td>
<td>59.1 ± 8.5</td>
<td>59.9 ± 8.1</td>
<td>0.12</td>
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<tr>
<td>Three vessel disease</td>
<td>330 (75.3)</td>
<td>349 (79.0)</td>
<td>0.20</td>
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<tr>
<td>EuroSCORE value</td>
<td>2.9 ± 2.0</td>
<td>3.0 ± 2.1</td>
<td>0.55</td>
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<tr>
<td>SYNTAX score value</td>
<td>24.2 ± 7.5</td>
<td>24.6 ± 8.1</td>
<td>0.47</td>
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Procedural Characteristics*

<table>
<thead>
<tr>
<th>PCI</th>
<th>464</th>
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<tbody>
<tr>
<td>Total stents number</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.4 ± 1.4</td>
</tr>
<tr>
<td>Total stent length, mm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>85.3 ± 38.2</td>
</tr>
<tr>
<td>Mean stent diameter, mm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.1 ± 0.3</td>
</tr>
<tr>
<td>IVUS guidance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>333 (71.8)</td>
</tr>
<tr>
<td>Complete revascularization</td>
<td></td>
</tr>
<tr>
<td></td>
<td>236 (50.9)†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CABG</th>
<th>401</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of grafted vessels</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.1 ± 0.9</td>
</tr>
<tr>
<td>Total no. of arterial grafts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.1 ± 1.1</td>
</tr>
<tr>
<td>Total no. of vein grafts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0 ± 0.8</td>
</tr>
<tr>
<td>Left internal mammary artery graft</td>
<td></td>
</tr>
<tr>
<td></td>
<td>398 (99.3)</td>
</tr>
<tr>
<td>Off-pump surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>258 (64.3)</td>
</tr>
<tr>
<td>Complete revascularization</td>
<td></td>
</tr>
<tr>
<td></td>
<td>274/383 (71.5)†</td>
</tr>
</tbody>
</table>

* Data were summarized according to the as-treated analysis
† P<0.05 between PCI and CABG group
Noninferiority Test for Primary End Point of 2-Year MACE

Prespecified non-inferiority margin: 4%

2-year MACE rate

<table>
<thead>
<tr>
<th></th>
<th>CABG: 11.0%</th>
<th>PCI: 7.9%</th>
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</thead>
<tbody>
<tr>
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</table>

Non-inferiority P=0.32

Absolute Risk Difference 3.1% points
95% CI -0.8-6.9

Difference (percentage point) of 2-year MACE rate (PCI – CABG)

Upper 1-sided 95% CI
Long-Term Follow-up
Primary End Point of MACE

Event rates were derived from Kaplan-Meier estimates.

Cumulative Incidence, %

Log-rank P=0.043

No. at Risk

- PCI
  - 438
  - 402
  - 362
  - 305
  - 242
  - 126

- CABG
  - 442
  - 415
  - 377
  - 326
  - 262
  - 145
Event rates were derived from Kaplan-Meier estimates.
Death

Event rates were derived from Kaplan-Meier estimates.

Cardiac Death: HR 1.15 (0.58-2.25), P=0.69
Non-Cardiac Death: HR 1.87 (0.69-5.05), P=0.21

Log-Rank P=0.30

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>PCI</th>
<th>CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>438</td>
<td>442</td>
</tr>
<tr>
<td>1</td>
<td>426</td>
<td>433</td>
</tr>
<tr>
<td>2</td>
<td>387</td>
<td>397</td>
</tr>
<tr>
<td>3</td>
<td>333</td>
<td>346</td>
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<tr>
<td>4</td>
<td>268</td>
<td>278</td>
</tr>
<tr>
<td>5</td>
<td>146</td>
<td>154</td>
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Cumulative Incidence, %

Years Since Randomization

5 10 15 20 25 30
Myocardial Infarction

Event rates were derived from Kaplan-Meier estimates.

Log-Rank $P=0.11$

<table>
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<tr>
<th>Years Since Randomization</th>
<th>PCI</th>
<th>CABG</th>
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<td></td>
<td>438, 419</td>
<td>442, 422</td>
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<tr>
<td></td>
<td>382, 325</td>
<td>386, 335</td>
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<tr>
<td></td>
<td>261, 140</td>
<td>271, 151</td>
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</tbody>
</table>
Event rates were derived from Kaplan-Meier estimates.
Myocardial Infarction

Percentages are crude rates throughout the available follow-up period

Crude Incidence, %

Periprocedural MI
- PCI: 0.7
- CABG: 1.1

P=0.48

Spontaneous MI
- PCI: 4.3
- CABG: 1.6

P=0.02

Percentages are crude rates throughout the available follow-up period.
CK-MB Elevation Post-Procedure

Percentages are crude rates throughout the available follow-up period.
Event rates were derived from Kaplan-Meier estimates
Any Repeat Revascularization

Cumulative Incidence, %

<table>
<thead>
<tr>
<th>Years Since Randomization</th>
<th>PCI</th>
<th>CABG</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>3.3%</td>
<td>0.5%</td>
</tr>
<tr>
<td>2</td>
<td>6.6%</td>
<td>1.5%</td>
</tr>
<tr>
<td>3</td>
<td>10.0%</td>
<td>2.5%</td>
</tr>
<tr>
<td>4</td>
<td>11.4%</td>
<td>3.6%</td>
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<tr>
<td>5</td>
<td>13.4%</td>
<td>6.6%</td>
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Log Rank P = 0.003

No. at Risk

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<th>PCI</th>
<th>438</th>
<th>393</th>
<th>335</th>
<th>257</th>
<th>164</th>
<th>80</th>
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<tr>
<td>CABG</td>
<td>442</td>
<td>414</td>
<td>365</td>
<td>286</td>
<td>189</td>
<td>87</td>
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Event rates were derived from Kaplan-Meier estimates
Target Lesion Revascularization

Event rates were derived from Kaplan-Meier estimates.

<table>
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<tr>
<th>Years Since Randomization</th>
<th>No. at Risk PCI</th>
<th>No. at Risk CABG</th>
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<tr>
<td>0</td>
<td>438</td>
<td>442</td>
</tr>
<tr>
<td>1</td>
<td>408</td>
<td>424</td>
</tr>
<tr>
<td>2</td>
<td>365</td>
<td>386</td>
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<tr>
<td>3</td>
<td>310</td>
<td>334</td>
</tr>
<tr>
<td>4</td>
<td>247</td>
<td>267</td>
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<tr>
<td>5</td>
<td>130</td>
<td>147</td>
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Log Rank P=0.19

Cumulative Incidence, %

PCI: 6.1%
CABG: 4.5%
New Lesion Revascularization

Event rates were derived from Kaplan-Meier estimates

<table>
<thead>
<tr>
<th>Years Since Randomization</th>
<th>No. at Risk PCI</th>
<th>No. at Risk CABG</th>
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<tr>
<td>0</td>
<td>438</td>
<td>442</td>
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<tr>
<td>1</td>
<td>416</td>
<td>427</td>
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<td>2</td>
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<td>389</td>
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<td>254</td>
<td>270</td>
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<tr>
<td>5</td>
<td>138</td>
<td>149</td>
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Log Rank P = 0.013

Cumulative Incidence, %

PCI: 6.5%
CABG: 2.4%
Event rates were derived from Kaplan-Meier estimates.
Definite or Probable Stent Thrombosis

Event rates were derived from Kaplan-Meier estimates.
## Long-Term Outcomes

<table>
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<tr>
<th>End points</th>
<th>PCI (N=464)</th>
<th>CABG (N=401)</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary End Points: MACE</strong></td>
<td>67 (15.3)</td>
<td>47 (10.6)</td>
<td>1.47 (1.01-2.13)</td>
<td><strong>0.043</strong></td>
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<tr>
<td><strong>Secondary End Points</strong></td>
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<tr>
<td>Death</td>
<td>29 (6.6)</td>
<td>22 (5.0)</td>
<td>1.34 (0.77-2.34)</td>
<td>0.30</td>
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<tr>
<td>Myocardial Infarction</td>
<td>21 (4.8)</td>
<td>12 (2.7)</td>
<td>1.76 (0.87-3.58)</td>
<td>0.11</td>
</tr>
<tr>
<td>Spontaneous MI</td>
<td>19 (4.3)</td>
<td>7 (1.6)</td>
<td>2.75 (1.16-6.54)</td>
<td><strong>0.017</strong></td>
</tr>
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<td>Stroke</td>
<td>11 (2.5)</td>
<td>13 (2.9)</td>
<td>0.86 (0.39-1.93)</td>
<td>0.72</td>
</tr>
<tr>
<td>Death, Myocardial Infarction, or stroke</td>
<td>52 (11.9)</td>
<td>42 (9.5)</td>
<td>1.26 (0.84-1.89)</td>
<td>0.26</td>
</tr>
<tr>
<td>Any Repeat Revascularization</td>
<td>48 (11.0)</td>
<td>24 (5.4)</td>
<td>2.09 (1.28-3.41)</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>Target Lesion Revascularization</td>
<td>25 (5.7)</td>
<td>17 (3.8)</td>
<td>1.51 (0.82-2.80)</td>
<td>0.19</td>
</tr>
<tr>
<td>New Lesion Revascularization</td>
<td>24 (5.5)</td>
<td>10 (2.3)</td>
<td>2.47 (1.18-5.17)</td>
<td><strong>0.013</strong></td>
</tr>
<tr>
<td>Death, MI, Stroke, or Any RR</td>
<td>87 (19.9)</td>
<td>59 (13.3)</td>
<td>1.54 (1.11-2.14)</td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
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<tr>
<td>TIMI Major Bleeding‡</td>
<td>30 (6.8)</td>
<td>132 (29.9)</td>
<td>0.20 (0.14-0.30)</td>
<td>&lt;<strong>0.001</strong></td>
</tr>
<tr>
<td>Fatal Bleeding</td>
<td>3 (0.7)</td>
<td>7 (1.6)</td>
<td>0.44 (0.11-1.68)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Percentages are crude rates throughout the available follow-up period.
## Subgroup Analysis for MACE

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Primary Outcome</th>
<th>Hazard Ratio (95% CI)</th>
<th>P value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCI</td>
<td>CABG</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n / total n. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>67/438 (15.3)</td>
<td>47/442 (10.6)</td>
<td>1.47 (1.01-2.13)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥65 yr</td>
<td>41/229 (17.9)</td>
<td>30/252 (11.9)</td>
<td>1.51 (0.95-2.42)</td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>26/209 (12.4)</td>
<td>17/190 (8.9)</td>
<td>1.43 (0.77-2.63)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>45/304 (14.8)</td>
<td>34/325 (10.5)</td>
<td>1.43 (0.92-2.24)</td>
</tr>
<tr>
<td>Female</td>
<td>22/134 (16.4)</td>
<td>13/117 (11.1)</td>
<td>1.53 (0.77-3.05)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td>2.24 (1.25-4.00)</td>
</tr>
<tr>
<td>Yes</td>
<td>34/177 (19.2)</td>
<td>17/186 (9.1)</td>
<td>1.07 (0.65-1.76)</td>
</tr>
<tr>
<td>No</td>
<td>33/261 (12.6)</td>
<td>30/256 (11.7)</td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td></td>
<td></td>
<td>1.30 (0.82-2.06)</td>
</tr>
<tr>
<td>Yes</td>
<td>40/228 (17.5)</td>
<td>33/238 (13.9)</td>
<td>1.89 (0.99-3.60)</td>
</tr>
<tr>
<td>No</td>
<td>27/210 (12.9)</td>
<td>14/204 (6.9)</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction</td>
<td></td>
<td></td>
<td>1.79 (0.51-6.21)</td>
</tr>
<tr>
<td>≤40%</td>
<td>7/17 (41.2)</td>
<td>4/17 (23.5)</td>
<td></td>
</tr>
<tr>
<td>&gt;40%</td>
<td>60/421 (14.3)</td>
<td>43/425 (10.1)</td>
<td></td>
</tr>
<tr>
<td>Vascular extent</td>
<td></td>
<td></td>
<td>1.43 (0.97-2.12)</td>
</tr>
<tr>
<td>3VD</td>
<td>56/330 (17.0)</td>
<td>42/349 (12.0)</td>
<td>1.45 (0.97-2.17)</td>
</tr>
<tr>
<td>2VD</td>
<td>11/108 (10.2)</td>
<td>5/93 (5.4)</td>
<td>1.89 (0.66-5.43)</td>
</tr>
<tr>
<td>SYNTAX score</td>
<td></td>
<td></td>
<td>1.59 (0.70-3.62)</td>
</tr>
<tr>
<td>Score ≥33</td>
<td>13/66 (19.7)</td>
<td>10/79 (12.7)</td>
<td></td>
</tr>
<tr>
<td>Score 23 - 32</td>
<td>30/187 (16.0)</td>
<td>14/177 (7.9)</td>
<td>2.14 (1.13-4.03)</td>
</tr>
<tr>
<td>Score ≤22</td>
<td>24/185 (13.0)</td>
<td>23/186 (12.4)</td>
<td>1.04 (0.59-1.84)</td>
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<tr>
<td>EuroSCORE</td>
<td></td>
<td></td>
<td>1.25 (0.55-2.84)</td>
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<tr>
<td>≥6</td>
<td>12/51 (23.5)</td>
<td>11/59 (18.6)</td>
<td></td>
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<tr>
<td>&lt;6</td>
<td>55/387 (14.2)</td>
<td>36/383 (9.4)</td>
<td>1.55 (1.02-2.35)</td>
</tr>
</tbody>
</table>

PCI better  CABG better
Diabetic Subgroup

**Death, MI, Stroke, or Repeat Revascularization**

- **HR (95%CI)**
  - Diabetes (n=363): 2.29 (1.35-3.87)
  - Non-diabetes (n=517): 1.16 (0.78-1.79)

**Death from any cause**

- **HR (95%CI)**
  - Diabetes (N=363): 1.25 (0.58-2.70)
  - Non-diabetes (N=517): 1.47 (0.66-3.28)

**Death, MI, or Stroke**

- **HR (95%CI)**
  - Diabetes (N=363): 1.46 (0.78-2.74)
  - Non-diabetes (N=517): 1.13 (0.66-1.93)

**Repeat Revascularization**

- **HR (95%CI)**
  - Diabetes (N=363): 4.31 (1.76-10.6)
  - Non-diabetes (N=517): 1.38 (0.75-2.53)

Percentages are crude rates throughout the available follow-up period.
Medication at Follow-Up

Aspirin

<table>
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<tr>
<th></th>
<th>DC</th>
<th>1Yr</th>
<th>2Yr</th>
<th>3Yr</th>
<th>4Yr</th>
<th>5Yr</th>
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<td>97</td>
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<td>94</td>
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Thienopyridine

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<th>4Yr</th>
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<td>97</td>
<td>89</td>
<td>88</td>
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<td>70</td>
<td>51</td>
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</table>

Statin

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<th>2Yr</th>
<th>3Yr</th>
<th>4Yr</th>
<th>5Yr</th>
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</thead>
<tbody>
<tr>
<td>%</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>83</td>
<td>90</td>
<td>87</td>
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</table>

Beta blocker

<table>
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<th>DC</th>
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<th>2Yr</th>
<th>3Yr</th>
<th>4Yr</th>
<th>5Yr</th>
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<tbody>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>69</td>
<td>43</td>
<td>89</td>
<td>65</td>
<td>54</td>
<td>50</td>
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</table>
As Treated Analysis
Noninferiority Test for Primary End Point of 2-Year MACE

<table>
<thead>
<tr>
<th>2-year MACE rate</th>
<th>CABG: 11.2%</th>
<th>PCI: 7.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prespecified non-inferiority margin: 4%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Non-inferiority P=0.44

Absolute Risk Difference 3.7% points
95% CI -0.2-7.6

Difference (percentage point) of 2-year MACE rate (PCI – CABG)

Upper 1-sided 95% CI
Primary End Point of MACE

Event rates were derived from Kaplan-Meier estimates.
# Long-Term Outcomes In As-Treated Analysis

<table>
<thead>
<tr>
<th>End points</th>
<th>PCI (N=464)</th>
<th>CABG (N=401)</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary End Points: MACE</strong></td>
<td>72 (15.5)</td>
<td>40 (10.0)</td>
<td>1.57 (1.07-2.31)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Secondary End Points</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>28 (6.0)</td>
<td>22 (5.5)</td>
<td>1.08 (0.62-1.89)</td>
<td>0.78</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>22 (4.7)</td>
<td>10 (2.5)</td>
<td>1.88 (0.89-3.97)</td>
<td>0.09</td>
</tr>
<tr>
<td>Spontaneous MI</td>
<td>20 (4.3)</td>
<td>5 (1.2)</td>
<td>3.43 (1.29-9.13)</td>
<td><strong>0.009</strong></td>
</tr>
<tr>
<td>Stroke</td>
<td>12 (2.6)</td>
<td>10 (2.5)</td>
<td>1.03 (0.45-2.39)</td>
<td>0.94</td>
</tr>
<tr>
<td>Death, Myocardial Infarction, or stroke</td>
<td>53 (11.4)</td>
<td>39 (9.7)</td>
<td>1.17 (0.77-1.77)</td>
<td>0.46</td>
</tr>
<tr>
<td>Any Repeat Revascularization</td>
<td>54 (11.6)</td>
<td>17 (4.2)</td>
<td>2.82 (1.64-4.87)</td>
<td><strong>&lt;0.001</strong></td>
</tr>
<tr>
<td>Target Lesion Revascularization</td>
<td>30 (6.5)</td>
<td>12 (3.0)</td>
<td>2.18 (1.12-4.26)</td>
<td>0.19</td>
</tr>
<tr>
<td>New Lesion Revascularization</td>
<td>27 (5.8)</td>
<td>6 (1.5)</td>
<td>3.93 (1.62-9.52)</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>Death, MI, Stroke, or Any RR</td>
<td>92 (19.8)</td>
<td>52 (13.0)</td>
<td>1.57 (1.12-2.20)</td>
<td><strong>0.009</strong></td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIMI Major Bleeding‡</td>
<td>23 (5.0)</td>
<td>139 (34.7)</td>
<td>0.12 (0.08-0.19)</td>
<td><strong>&lt;0.001</strong></td>
</tr>
<tr>
<td>Fatal Bleeding</td>
<td>5 (1.1)</td>
<td>5 (1.2)</td>
<td>0.85 (0.25-2.94)</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Percentages are crude rates throughout the available follow-up period.
Conclusion

• The BEST trial failed to show that PCI with everolimus-eluting stents was noninferior to CABG with respective to the primary end point of death, myocardial infarction, or target vessel revascularization at 2 years.

• At longer-term follow-up (median 4.6 years), PCI was associated with a significant increase in the incidence of the primary end point compared with CABG.
Trial of Everolimus-Eluting Stents or Bypass Surgery for Coronary Disease

Seung-Jung Park, M.D., Ph.D., Jung-Min Ahn, M.D., Young-Hak Kim, M.D., Duk-Woo Park, M.D., Sung-Cheol Yun, Ph.D., Jong-Young Lee, M.D., Soo-Jin Kang, M.D., Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Seong-Wook Park, M.D., Suk Jung Choo, M.D., Cheol Hyun Chung, M.D., Jae Won Lee, M.D., David J. Cohen, M.D., Alan C. Yeung, M.D., Seung Ho Hur, M.D., Ki Bae Seung, M.D., Tae Hoon Ahn, M.D., Hyuck Moon Kwon, M.D., Do-Sun Lim, M.D., Seung-Woon Rha, M.D., Myung-Ho Jeong, M.D., Bong-Ki Lee, M.D., Damras Tresukosol, M.D., Guo Sheng Fu, M.D., and Tiong Kiam Ong, M.D., for the BEST Trial Investigators*
## Reasons for Screening Failure for Enrollment

<table>
<thead>
<tr>
<th>Reasons</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main stenosis</td>
<td>766</td>
</tr>
<tr>
<td>Concurrent enrollment in another clinical trial</td>
<td>639</td>
</tr>
<tr>
<td>CTO $\geq 2$ in major epicardial coronary artery</td>
<td>248</td>
</tr>
<tr>
<td>Planned surgical procedure other than CABG</td>
<td>235</td>
</tr>
<tr>
<td>Prior CABG surgery</td>
<td>209</td>
</tr>
<tr>
<td>Acute ST-elevation MI (Q-wave) within 72 hours</td>
<td>253</td>
</tr>
<tr>
<td>Prior PCI with DES implantation within 1 year</td>
<td>192</td>
</tr>
<tr>
<td>Elevated cardiac enzymes at time of randomization</td>
<td>145</td>
</tr>
<tr>
<td>Serious extra-cardiac illness</td>
<td>100</td>
</tr>
<tr>
<td>Heart failure (NYHA class III or IV)</td>
<td>83</td>
</tr>
<tr>
<td>Previous stroke within 6 months</td>
<td>30</td>
</tr>
<tr>
<td>Prior history of significant bleeding ($&lt; 6$ months)</td>
<td>10</td>
</tr>
<tr>
<td>Not possible to access the research center</td>
<td>7</td>
</tr>
<tr>
<td>Hypersensitivity or contraindication to medication</td>
<td>6</td>
</tr>
<tr>
<td>Intolerance to antiplatelet agent</td>
<td>6</td>
</tr>
</tbody>
</table>
Event rates were derived from Kaplan-Meier estimates.
Event rates were derived from Kaplan-Meier estimates.

Cumulative Incidence, %

Years Since Randomization

0-30 days: HR, 0.62 (95% CI, 0.26-1.49), P=0.28
>30 days: HR, 1.69 (95% CI, 0.98-2.91), P=0.054

PCI
CABG

9.6%
5.5%
## Repeat Revascularization

<table>
<thead>
<tr>
<th>Target Vessel (N=48)</th>
<th>Non-Target Vessel (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target Lesion</strong> (N=36)</td>
<td></td>
</tr>
<tr>
<td><strong>Target Lesion plus New Lesion</strong> (N=6)</td>
<td></td>
</tr>
<tr>
<td><strong>New Lesion</strong> (N=4)</td>
<td></td>
</tr>
<tr>
<td><strong>Unknown</strong> (N=2)</td>
<td></td>
</tr>
</tbody>
</table>
## Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>PCI (N=438)</th>
<th>CABG (N=442)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>64.0 ± 9.3</td>
<td>64.9 ± 9.4</td>
<td>0.13</td>
</tr>
<tr>
<td>Male sex</td>
<td>304 (69.4)</td>
<td>325 (73.5)</td>
<td>0.18</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.7 ± 2.9</td>
<td>2.0 ± 2.9</td>
<td>0.16</td>
</tr>
<tr>
<td>Diabetes</td>
<td>177 (40.4)</td>
<td>186 (42.1)</td>
<td>0.62</td>
</tr>
<tr>
<td>Hypertension</td>
<td>296 (67.6)</td>
<td>295 (66.7)</td>
<td>0.79</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>239 (54.6)</td>
<td>222 (50.2)</td>
<td>0.20</td>
</tr>
<tr>
<td>Current smoker</td>
<td>88 (20.1)</td>
<td>89 (20.1)</td>
<td>0.99</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>30 (6.8)</td>
<td>38 (8.6)</td>
<td>0.33</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>25 (5.7)</td>
<td>29 (6.6)</td>
<td>0.60</td>
</tr>
<tr>
<td>Previous congestive heart failure</td>
<td>16 (3.7)</td>
<td>12 (2.7)</td>
<td>0.43</td>
</tr>
</tbody>
</table>
## Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>PCI (N=438)</th>
<th>CABG (N=442)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic renal failure</td>
<td>9 (2.1)</td>
<td>7 (1.6)</td>
<td>0.60</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>15 (3.4)</td>
<td>12 (2.7)</td>
<td>0.54</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>8 (1.8)</td>
<td>6 (1.4)</td>
<td>0.58</td>
</tr>
<tr>
<td>Clinical manifestation</td>
<td></td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td>Stable angina or asymptomatic</td>
<td>210 (47.9)</td>
<td>204 (46.2)</td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td>185 (42.2)</td>
<td>199 (45.0)</td>
<td></td>
</tr>
<tr>
<td>Recent acute myocardial infarction</td>
<td>43 (9.8)</td>
<td>39 (8.8)</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>59.1 ± 8.5</td>
<td>59.9 ± 8.1</td>
<td>0.12</td>
</tr>
<tr>
<td>Three vessel disease</td>
<td>330 (75.3)</td>
<td>349 (79.0)</td>
<td>0.20</td>
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<tr>
<td>EuroSCORE value</td>
<td>2.9 ± 2.0</td>
<td>3.0 ± 2.1</td>
<td>0.55</td>
</tr>
<tr>
<td>SYNTAX score value</td>
<td>24.2 ± 7.5</td>
<td>24.6 ± 8.1</td>
<td>0.47</td>
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