PLATINUM Diversity:
Outcomes with the Promus PREMIER™ Stent in Women and Minorities
Long Term Outcomes After PCI with PES in Black Versus White Patients

Black vs. White:
Risk of MI and Stent Thrombosis

Batchelor et al. J Interv Cardiol 2012
Disparities in Clinical Research Mirror those in Clinical Practice

Women comprise 30% of PCI procedures and PCI clinical trial enrollment.

PCI Procedures 2009

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAXUS-IV</td>
<td>72%</td>
<td>28%</td>
</tr>
<tr>
<td>SPIRIT III</td>
<td>69%</td>
<td>31%</td>
</tr>
<tr>
<td>SIRIUS</td>
<td>71%</td>
<td>29%</td>
</tr>
<tr>
<td>ENDEAVOR</td>
<td>77%</td>
<td>23%</td>
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</tbody>
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Gender representation in PCI clinical trials

Current Clinical Enrollees do not Reflect the US Population

People of color are projected to outnumber U.S. white population by 2042.

U.S. population 18–24 years old, by race/ethnicity: July 1990–99 and projections to 2050

Composition (%)

Registry
US

Male
Female

White
86
72

Other
0.8
6

Pacific
0.16
0.2

AI/AN
0.2
0.9

Asian
0.5
5

Latino
4
16

Black
7.5
13

Other
4
16

Composition (%)

N=5305

Sources: U.S. Bureau of the Census
U.S. Census Bureau, 2009 National Projections supplement to the 2008 National Projections, August 14, 2008
### Key Environmental Drivers of the Need for Increased Diversity in Clinical Trials

<table>
<thead>
<tr>
<th>SCIENTIFIC</th>
<th>ETHICAL</th>
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<tbody>
<tr>
<td>Testing the safety and effectiveness of new medicines should accurately reflect the changing demographic of the patient population that will eventually take them.</td>
<td>Clinical trials in which minorities are underrepresented may not adequately serve the health needs of these communities.</td>
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</tbody>
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<thead>
<tr>
<th>REGULATORY</th>
<th>COMMERCIAL</th>
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<tr>
<td>Both domestically and internationally, Regulators and other stakeholders are demanding more data from diverse populations.</td>
<td>Delays in recruitment cost billions and keeps novel therapies away from the patients that will benefit from them.</td>
</tr>
</tbody>
</table>

Clinical Trial Engagement Network  
National Minority Quality Forum, 2014
Study Design

**Study Objective:**
To compile acute procedural performance and clinical outcomes data for the Promus PREMIER EES in understudied/underserved patient populations including women and minorities

- **Enrollment:** 1500 patients / Up to 65 US Sites
- **Primary Investigators:**
  - Wayne Batchelor: Florida State College of Medicine, Tallahassee Research Institute, & Southern Medical Group, Tallahassee, FL
  - Roxana Mehran: Icahn School of Medicine at Mount Sinai Hospital, New York, NY

- Observational
- Prospective
- Multicenter
- Open-label
- Single-arm

≥ 1 PREMIER Stent & one or more of the following:
  - Female
  - Black
  - Hispanic/Latino
  - American Indian or Alaskan Native

Follow-up (telephone):
- 30 days
- 6 months
- 1 year

Primary Endpoint:
- 12M Death/MI/TVR

Demographic collection on socioeconomic status, level of education, insurance status, language, etc.
Adherence to DAPT

Aligned with Close The Gap educational initiative to address disparities in cardiovascular care for women and minorities
PLATINUM Diversity
Study Design: Statistical Analysis

| Primary Statistical Hypothesis | Patients combined from PE+ Post Approval Study and PLATINUM Diversity:  
|                               | • Female patients  
|                               | • Minority patients (Black of African Heritage, Hispanic/Latino, American Indian or Alaska native)  
|                               | vs. Reference subset of Caucasian male patients from the PE+ PAS  
| H_0: P_{PE+} = P_{SG} (Not Superior)  
| H_1: P_{PE+} ≠ P_{SG} (Superior)  

| Statistical Test Method | • Multivariate logistic regression model  
|                        | • Adjusting for the baseline covariate imbalance  

| Statistical Power | • Enrollment of patients from specific subgroups will be monitored/stopped as needed to ensure sufficient enrollment in other subgroups  
|                  | • IF female patient cohort 12-month Death/MI/TVR rate of 10.1%  
|                  |   • 80% power to detect a significant difference between PE+ Caucasian male patients and the combined PE+ and PLATINUM Diversity female patients  
|                  | • IF the combined minority patient cohort has a 12-month Death/MI/TVR rate of 10.6%  
|                  |   • 80% power to detect a significant difference between PE+ Caucasian male patients and the combined PE+ and PLATINUM Diversity minority patients  

Thank you.
Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

Indications for Use:
The Promus PREMIER Everolimus-Eluting Platinum Chromium Coronary Stent System is indicated for improving luminal diameter in patients with symptomatic heart disease or documented silent ischemia due to de novo lesions in native coronary arteries ≥2.25 mm to ≤4.00 mm in diameter in lesions ≤34 mm in length.

Contraindications:
Use of the Promus PREMIER Everolimus-Eluting Platinum Chromium Coronary Stent System is contraindicated in patients with known hypersensitivity to:
- 316L stainless steel or platinum
- everolimus or structurally-related compounds
- the polymers or their individual components (see Section 2.2.2, Primer Polymer and Drug Matrix Copolymer Carrier)

Coronary Artery Stenting is contraindicated for use in:
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device
- Patients with uncorrected bleeding disorders or patients who cannot receive anticoagulation or antiplatelet aggregation therapy (see Section 6.2, Pre- and Post-Procedural Antiplatelet Regimen for more information).

Warnings:
- To maintain sterility, the inner package should not be opened or damaged prior to use.
- The use of this product carries the risks associated with coronary artery stenting, including stent thrombosis, vascular complications, and/or bleeding events.
- This product should not be used in patients who are not likely to comply with recommended antiplatelet therapy.

Precautions:
- Only physicians who have received adequate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent stent blockage may require repeat dilation of the arterial segment containing the stent. The long-term outcome following repeat dilation of endothelialized stents is not well characterized.
- Consideration should be given to the risks and benefits of use in patients with history of severe reaction to contrast agents.
- Do not expose the delivery system to organic solvents such as alcohol or detergents.
- Care should be taken to control the position of the guide catheter tip during stent delivery, deployment and balloon withdrawal. Before withdrawing the stent delivery system, visually confirm complete balloon deflation by fluoroscopy to avoid guiding catheter movement or damage to the stent struts during withdrawal.
- Stent thrombosis is a low-frequency event that current drug-eluting stent (DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with myocardial infarction (MI) or death. In the clinical trials analyzed to date, differences in the incidence of stent thrombosis have not been associated with an increased risk of cardiac death, MI, or all-cause mortality. Additional data from longer-term follow-up of the PLATINUM clinical trials and analyses of stent thrombosis related to DES are expected and should be considered in making treatment decisions as data become available.
- When DES are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the NG PROMUS and PLATINUM pivotal clinical trials.
- Compared to use within the specified Indications for Use, the use of DES in patients and lesions outside of the labeled indications may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI or death.
- Orally-administered everolimus combined with cyclosporine is associated with increased serum cholesterol and triglyceride levels.

The safety and effectiveness of the Promus PREMIER Stent have not been established in the cerebral, carotid, or peripheral vasculature or in the following patient populations:
- Patients requiring multiple stents patients with prior brachytherapy of the target lesion or in patients with history of severe reaction to contrast agents.
- Patients with vessel thrombus at the lesion site.

Use of the Promus PREMIER Everolimus-Eluting Platinum Chromium Coronary Stent System is contraindicated in patients with:
- Recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with coronary artery reference vessel diameters <2.25 or >4.00 mm.
- Patients with coronary artery lesions longer than 34 mm or requiring more than one Promus PREMIER Stent.
- Patients with lesions located in the saphenous vein grafts, in the left main coronary artery, ostial lesions, or lesions located at a bifurcation. Patients with diffuse disease or poor flow distal to the lesion or who have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.
- Patients with coronary artery reference vessel diameters ≥2.25 mm to ≤4.00 mm in lesions ≤34 mm in length.
- Patients with moderate or severe calcification in the lesion or a chronic total occlusion. Patients with 3 vessel disease.

9.2 Potential Adverse Events
Potential adverse events (in alphabetical order) which may be associated with the use of a coronary stent in native coronary arteries include but are not limited to:
- Abrupt stent closure
- Acute myocardial infarction
- Allergic reaction to anti-coagulant and/or antiplatelet therapy, contrast medium, or stent materials
- Angina
- Arhythmias, including ventricular fibrillation and ventricular tachycardia
- Arteriovenous fistula
- Bleeding
- Cardiac tamponade
- Cereidogenic shock/pulmonary edema
- Coronary aneurysm
- Death
- Dissection
- Emboli, distal (air, tissue or thrombotic material or material from device(s) used in the procedure)
- Heart failure
- Hematoma
- Hemorrhage, which may require transfusion
- Hypertension
- Infection, local or systemic
- Ischemia
- Myocardial
- Pain, access site
- Perforation or rupture of coronary artery
- Pericardial effusion
- Pseudaneurysm
- Renal insufficiency or failure
- Respiratory failure
- Restenosis of stented segment
- Stent embolization or migration
- Stent deformation, collapse, or fracture
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident/transient ischemic attack
- Total occlusion of coronary artery
- Vessel spasm
- Vessel trauma requiring surgical repair or intervention

The following list includes the known risks of everolimus on the oral doses listed above. The amount of drug that circulates in the bloodstream following implantation of a Promus PREMIER™ Stent is several folds lower than that obtained with oral doses (1.5 mg to 20 mg/day, see Section 7.2, Pharmacokinetics).
- Abdominal pain (including upper abdominal pain)
- Anemia
- Angioedema
- Anorexia
- Asthenia
- Constipation
- Cough
- Delayed wound healing/liquid accumulation
- Diarrhea
- Dyslipidemia (including hyperlipidemia and hypercholesterolemia)
- Dry mouth
- Dyspepsia
- Dysuria
- Ear pain
- Edema
- Epilepsy
- Fatigue
- Headache
- Hematuria
- Hyperglycemia (may include new onset of diabetes)
- Hyperkalemia
- Hypertension
- Hypothyroidism
- Hypoglycemia
- Hypophosphatemia
- Increased serum creatinine
- Infections and serious infections: bacterial, viral, fungal, and protozoal infections (may include herpes virus infection, polychromatophilic leukocytosis which may be associated with BK virus infection, and/or other opportunistic infections)
- Insomnia
- Interaction with strong inhibitors and inducers of CYP3A4
- Leukopenia
- Lymphoma and other malignancies (including skin cancer)
- Male infertility (azospermia and/or oligospermia)
- Mucosal inflammation (including oral ulceration and oral mucositis)
- Mucous membrane irritation
- Myasthenia
- Nausea
- Neutropenia
- Non-infectious pneumonitis
- Pain, extremity, incision site and procedural, back, chest, muscle/eskeletal
- Proteinuria
- Pyrexia
- Rash
- Stomatitis
- Thrombocytopenia
- Thrombotic microangiopathy (TMA)
- Thrombotic thrombocytopenic purpura (TTP)
- Hereditary angioedema syndrome (HAE)
- Tremor
- Upper respiratory tract infection
- Urinary tract infection
- Vomiting

Live vaccines should be avoided and close contact with those that have had live vaccines should be avoided. Fetal harm can occur when administered to a pregnant woman. There may be other potential adverse events that are unforeseen at this time.

Prior to use, please refer to the Instructions for Use at www.bostonscientific.com for more information on indications, contraindications, warnings, precautions, and adverse events.