A Post-Approval Study of the PROMUS PREMIER™ Everolimus-Eluting Platinum Chromium Coronary Stent System in China

PROMUS PREMIER™ China Post-Approval Study

CLINICAL PROTOCOL

Study Reference # S2384

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2. Protocol Synopsis

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Study Objective(s)	To compile real-world clinical outcome data for the Promus PREMIER™ Everolimus-Eluting Platinum Chromium Coronary Stent System (Promus PREMIER™ Stent System) in routine clinical practice in China.
Planned indication for use	The PROMUS PREMIER™ Stent System is indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete de novo native coronary artery lesions.
Test Device	Promus PREMIER™ Monorail Everolimus-Eluting Platinum Chromium Coronary Stent System (Promus PREMIER™ Stent System)
Control Device	No control arm
Device Sizes	Promus PREMIER™ Stents are available in the following sizes in China (stent diameter x stent length): 2.25 mm x 8, 12, 16, 20, 24, 28, 32 mm 2.50 mm x 8, 12, 16, 20, 24, 28, 32, 38 mm 2.75 mm x 8, 12, 16, 20, 24, 28, 32, 38 mm 3.00 mm x 8, 12, 16, 20, 24, 28, 32, 38 mm 3.50 mm x 8, 12, 16, 20, 24, 28, 32, 38 mm 4.00 mm x 8, 12, 16, 20, 24, 28, 32, 38 mm
Study Design	A prospective, open-label, multi-center study designed to observe clinical outcomes in subjects receiving the Promus PREMIER™ Stent System.
Study Population	All subjects who are candidates for coronary artery stenting, signed the informed consent form and eligible to receive a Promus PREMIER™ Stent System will be evaluated for enrollment in this study.
Planned Number of Subjects	At least 2000 subjects will be enrolled. Each site will be allowed to enroll up to a maximum of 300 subjects.
Planned Number of Investigational Sites / Countries	Up to 25 investigational sites in China
Primary Endpoint	The primary endpoint is the 12-month major adverse cardiac event (MACE) rate, defined as cardiac death, myocardial infarction (MI) and target vessel

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	revascularization (TVR)
Additional Endpoints	Secondary endpoints will be analyzed for all subjects at 30 days, 6 months, 12 months and then annually through 5 years post stent implant. • Stent Thrombosis (ST) rate using Academic Research Consortium (ARC) definition (definite/probable) • MACE rates (at 30-day, 6-month and 2 – 5 years annually) • Target lesion failure (TLF) rate, defined as any ischemia-driven revascularization of the target lesion (TLR), MI (Q-wave and non–Q-wave) related to the target vessel, or cardiac death • TLR Rate • TVR Rate • Cardiac death or MI rate • Cardiac death rate • MI rate • Non-cardiac death rate • All death rate • All death or MI rate
Method of Assigning patients to Treatment	Each enrolled patient will receive Promus PREMIER™ Stent System(s)
Follow-up Schedule	Subject follow up will occur via telephone contact or clinic visit at 30 days, 6 months, 12 months and then annually through 5 years post stent implant, for all enrolled subjects. Enrolled subjects with a Promus PREMIER™ Stent implant failure will be followed through hospital discharge following the initial attempted index procedure.
Study Duration	Approximately 6 years
Recommended Antiplatelet Therapy	Based on the American College of Cardiology (ACC)/American Heart Association (AHA)/Society for Cardiovascular Angiography and Interventions (SCAI) guidelines[ab], and supported by the European Society of Cardiology (ESC) guidelines[c], dual antiplatelet therapy with aspirin and a clopidogrel is prescribed as follows to reduce the risk of thrombosis.

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	Aspirin Subjects must be treated with aspirin indefinitely after the index procedure. **Thienopyridine** • For subjects who have been taking clopidogrel for ≥72 hours at the time of the index procedure, a loading dose is not required. • For subjects who have not been taking clopidogrel for ≥72 hours at the time of the index procedure, a loading dose is required. It is recommended that the loading dose be administered prior to the index procedure. However, in all cases, the loading dose is required to be administered not more than 2 hours after the index procedure. The following loading doses are recommended: o Clopidogrel: A peri-procedural loading dose of 600 mg is recommended. • Subjects must be treated with clopidogrel for at least 6 months following the index procedure. In subjects not at high risk of bleeding, clopidogrel treatment should continue for at least 12 months following the index procedure. a: Levine GN, Bates ER, Blankenship JC, et al. Circulation 2011 ;124 :e574-e651. b: Wijns W, Kolh P, Danchin N, et al. Eur Heart J 2010; 31:2501-2555. c: Wright, R.S., et al., J Am Coll Cardiol, 2011. **57**(19): p. e215-367.
Subsets	This study will capture usage patterns and assess clinical outcomes in real-world subject populations. Pre-specified subject and lesion subsets to include, but not be limited to: • Lesions in the setting of ST elevation myocardial infarction (STEMI) • Subjects with acute coronary syndrome/unstable angina • Long lesions • Multiple overlapping stents • Bifurcation lesions • Subjects with diabetes • Subjects with renal insufficiency • Subjects with 2 or 3 vessels treated • Left main (LM) lesions • Subjects with chronic total occlusions (CTO) • Stenting of vein grafts • In-stent restenosis (ISR) • Subjects with left ventricular dysfunction with ejection fraction (EF) < 25% • Subjects with reference vessel diameter (RVD) < 2.5mm • Male gender • Female gender • Subjects with simple lesions*

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	• Subjects with complex lesions Subgroup analyses will be performed only if the subgroup size is at least 100 subjects. *The subjects with simple lesions cohort has been defined as all subjects without acute MI, graft stenting, chronic total occlusion, ISR, failed brachytherapy, bifurcation, ostial lesion, severe tortuosity, moderate or severe calcification by visual estimate in target lesion or target vessel proximal to target lesion, three-vessel stenting, cardiogenic shock, left main disease, or acute or chronic renal dysfunction (serum creatinine > 2.0 mg/dl or subject on dialysis). For the subjects with simple lesions, lesion length and RVD should meet one of two following criteria: 1). lesion length ≤ 28 mm and diameter ≥ 2.25 mm and < 2.5 mm, or 2). lesion length ≤ 24 mm and diameter ≥ 2.5 mm and ≤ 4.25 mm.
Key Inclusion Criteria	• Subject must be at least 18 years of age • Subject understands and provides written informed consent • Subject who is clinically indicated and will have an attempt of at least one Promus PREMIER™ Stent OR Subject who is clinically indicated and was implanted with at least one Promus PREMIER™ Stent • Subject is willing to comply with all protocol-required follow-up evaluation
Key Exclusion Criteria	Exclusion criteria are not required in the PE PREMIER™ China Post-Approval Study which is an “all comers” study.
Statistical Methods	Descriptive statistics will be performed for key variables collected in the study. The detail will be documented in the statistical analysis plan (SAP).
Safety Parameters	All serious adverse events (SAE), adverse device effects (ADE), major adverse cardiac events (MACE) and stent thrombosis will be collected up to 5 years follow-up intervals. A clinical events committee (CEC) will adjudicate for MACE and stent thrombosis through the 5-year follow- up.