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Polymer-Based, Paclitaxel-Eluting TAXUS Liberté Stent in De Novo Lesions

The Pivotal TAXUS ATLAS Trial

Mark A. Turco, MD,* John A. Ormiston, MBChB,† Jeffrey J. Popma, MD,‡ Lazar Mandinov, MD,§ Charles D. O'Shaughnessy, MD,‖ Tift Mann, MD,¶ Thomas F. McGarry, MD,# Chiung-Jen Wu, MD,** Charles Chan, MD,†† Mark W. I. Webster, MBChB,‡‡ Jack J. Hall, MD,§§ Gregory J. Mishkel, MD,‖‖ Louis A. Cannon, MD,¶¶ Donald S. Baim, MD,§ Joerg Koglin, MD§

Takoma Park, Maryland; Auckland, New Zealand; Boston and Marlborough, Massachusetts; Elyria, Ohio; Raleigh, North Carolina; Oklahoma City, Oklahoma; Kaohsiung, Taiwan; Singapore; Indianapolis, Indiana; Springfield, Illinois; and Petoskey, Michigan

Objectives The goal of this research was to assess non-inferiority of the next-generation TAXUS Liberté stent (Boston Scientific Corp., Natick, Massachusetts) versus the TAXUS Express stent (Boston Scientific Corp.).

Background The introduction of drug-eluting stents (DES) has shifted clinical practice towards more complex lesion subsets, prompting the need for more deliverable DES. TAXUS Liberté was designed to combine the established polymer-based, paclitaxel-elution TAXUS technology with the more advanced Liberté stent platform.

Methods The TAXUS ATLAS study is a global, prospective, single-arm trial evaluating outcomes in de novo coronary lesions visually estimated to be 10 to 28 mm in length in vessels 2.5 to 4.0 mm in diameter. The control group is an entry-criteria-matched population of TAXUS Express patients from the TAXUS IV and V trials. The primary end point is non-inferiority of TAXUS Liberté versus TAXUS Express for 9-month target vessel revascularization.

Results Despite similar inclusion criteria, quantitative coronary angiography-determined baseline lesion characteristics were significantly more complex for TAXUS Liberté than TAXUS Express. The primary non-inferiority end point was met with the 1-sided 95% confidence bound of 2.98% less than the pre-specified non-inferiority margin of 3% ($p = 0.0487$).

Conclusions Despite the treatment of more complex lesions with TAXUS Liberté, the primary end point was met, demonstrating that TAXUS Liberté is non-inferior to TAXUS Express. The successful transfer of the proven TAXUS technology to the more advanced TAXUS Liberté platform was demonstrated. (TAXUS ATLAS: TAXUS Liberté-SR Stent for the Treatment of De Novo Coronary Artery Lesions; http://www.clinicaltrials.gov/ct/show/NCT00371709?order=1; NCT00371709) (J Am Coll Cardiol 2007;49:1676–83) © 2007 by the American College of Cardiology Foundation

From the *Center for Cardiac & Vascular Research, Washington Adventist Hospital, Takoma Park, Maryland; †Mercy Angiography Unit, Mercy Hospital, Auckland, New Zealand; ‡Department of Internal Medicine (Cardiovascular Division), Brigham and Women's Hospital, Boston, Massachusetts; §Boston Scientific Corporation, Marlborough, Massachusetts; ‖Elyria Memorial Hospital, Elyria, Ohio; ¶Wake Heart Associates, Wake Medical Center, Raleigh, North Carolina; #Oklahoma Foundation for Cardiovascular Research, Oklahoma Heart Hospital, Oklahoma City, Oklahoma; **Cardiology Section, Chang-Gung Memorial Hospital, Kaohsiung, Taiwan; ††National Heart Centre, Singapore, Singapore; ‡‡Cardiac Investigations Unit, Auckland City Hospital, Auckland, New Zealand; §§The Heart Center, St. Vincent's Hospital, Indianapolis, Indiana; ‖‖Prairie Heart Institute, St. John's Hospital, Springfield, Illinois; and the ¶¶Cardiac & Vascular Research Center, Northern Michigan Hospital, Petoskey, Michigan. This study was supported by Boston Scientific Corporation, Natick, Massachusetts. Dr. Turco has received consulting fees/honoraria, is on the Speakers' Bureau, and has received research grants from Boston Scientific Corporation. Dr. Ormiston has received consulting fees/honoraria and is on the Advisory Board of Boston Scientific Corporation. Dr. O'Shaughnessy has received consulting fees/honoraria and is on the Speakers' Bureau and the Advisory Board of Boston Scientific Corporation. Dr. Chan has received consulting fees/honoraria, is on the Speakers' Bureau, and has received research grants from Boston Scientific Corporation. Dr. Mishkel has received consulting fees/honoraria, is on the Speakers' Bureau, and has received research grants from Boston Scientific Corporation. Dr. Cannon is on the Speakers' Bureau of Boston Scientific Corporation. Drs. Popma and Webster have received research grants from Boston Scientific Corporation. Dr. Ormiston is on the Advisory Board of Boston Scientific Corporation. Dr. Baim is a stockholder and full-time employee of Boston Scientific Corporation. Dr. McGarry is a stockholder of Boston Scientific Corporation. Drs. Mandinov and Koglin are full-time employees of Boston Scientific Corporation.

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The effectiveness of first-generation drug-eluting stents (DES) in reducing restenosis after percutaneous coronary intervention has been established (1–3). While reducing restenosis in all lesion and patient populations studied, the use of first-generation DES in more complex lesions has been limited by stent design.

The next-generation TAXUS Liberté (Boston Scientific Corp., Natick, Massachusetts) paclitaxel-eluting stent platform was developed to improve deliverability, conformability, and drug distribution homogeneity while maintaining the established antirestenotic properties of the TAXUS polymer-based, paclitaxel-elution technology. Since both stents use the same drug-eluting technology, we hypothesized that TAXUS Liberté would be as safe and effective as TAXUS Express (Boston Scientific Corporation) while being more deliverable. Therefore, we initiated the prospective, single-arm, non-inferiority TAXUS ATLAS trial to evaluate the safety and efficacy of TAXUS Liberté versus historical TAXUS Express controls in single, de novo coronary lesions.

Methods

Device description. Both TAXUS Express^2-SR and TAXUS Liberté-SR consist of a balloon-expandable stent with a polymer coating containing 1 $\mu g/mm^2$ of paclitaxel in a slow-release formulation on the Express or Liberté platforms, respectively (Fig. 1).

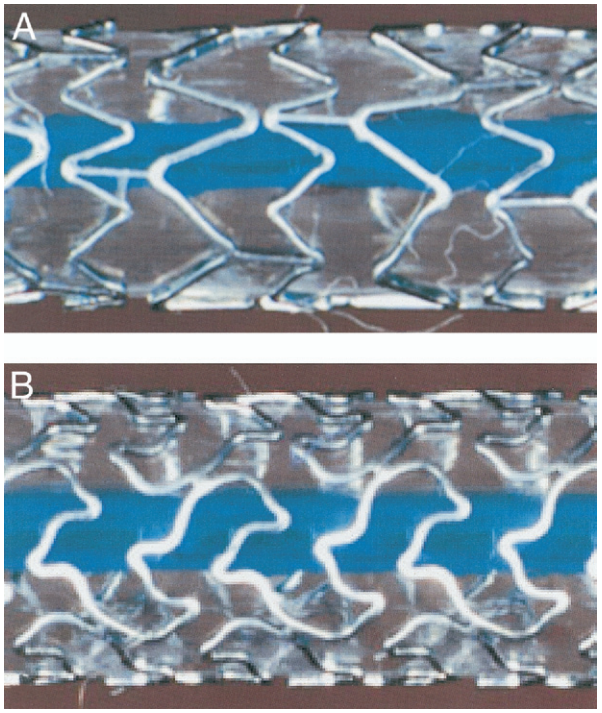

Figure 1 Study Devices

(A) TAXUS Express. **(B)** TAXUS Liberté.

Abbreviations and Acronyms

DES = drug-eluting stent(s)
ITT = intention-to-treat
MACE = major adverse cardiac events
MI = myocardial infarction
MLD = minimum lumen diameter
PP = per protocol
QCA = quantitative coronary angiography
TVR = target vessel revascularization

Patient selection and study flow. A total of 871 patients were enrolled at 61 centers in 7 countries in North America and Asia Pacific from August 2004 to February 2005 to receive the TAXUS Liberté stent. Eligible patients were ≥18 years old with a single de novo lesion ≥10 and ≤28 mm in length (by visual estimate) in a native coronary artery with a reference vessel diameter of ≥2.5 and ≤4.0 mm (by visual estimate). Patients with acute (<72 h) myocardial infarction (MI), left main disease, ostial or bifurcation lesions, total occlusion or thrombus, calcification, or tortuosity were excluded. Additional study stents were allowed in the target lesion when clinically indicated for bailout reasons. The study protocol was approved by local ethics review committees. All patients provided written informed consent.

Loading doses of clopidogrel (300 mg) or ticlopidine (500 mg) and aspirin (300 mg) were administered before stent implantation. After implantation, all patients were prescribed clopidogrel (75 mg daily) or ticlopidine (250 mg twice daily) for a minimum of 6 months, and aspirin (≥100 mg daily) for at least 9 months but recommended indefinitely.

Clinical follow-up was scheduled at 1, 4, and 9 months and yearly thereafter for 5 years. Follow-up quantitative coronary angiography (QCA) and intravascular ultrasound were scheduled at 9 months for a randomized subset of patients (Fig. 2A).

Control group. The control group consisted of a historical population of TAXUS Express-SR patients from the TAXUS IV and V trials (2,3); inclusion and exclusion criteria were similar to those for the TAXUS ATLAS trial (Fig. 2B).

Data management and definitions. Independent monitors verified all data from case report forms. Stent thrombosis, death, and major adverse cardiac events (MACE), including cardiac death, MI, and target vessel revascularization (TVR), were adjudicated by an independent Clinical Events Committee. A data monitoring committee periodically reviewed safety data. The clinical and angiographic end point definitions were identical to those in the TAXUS IV and V trials (2,3).

Blinded angiographic analysis was performed using validated quantitative methods (4). The same core lab (Brigham and Women's Hospital, Boston, Massachusetts) and procedures were used as for the TAXUS IV and V trials.

Pre-specified non-inferiority end points. The primary end point was 9-month TVR. In-stent percent diameter stenosis, binary restenosis, minimum lumen diameter (MLD), and late loss were also tested for non-inferiority.