Results from the OPTIMIZE trial reported

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The OPTIMIZE randomized trial comparing a novel, low-profile drug-eluting stent (DES) facilitating transradial access (TR) and direct stenting (DS) to existing DES did not establish non-inferiority of the new stent based on the prespecified study statistical analysis plan, likely due to the definition of periprocedural target vessel myocardial infarction (TVMI) coupled with a large proportion of high-sensitive cardiac troponin assays used in the trial.

Findings were reported today at TCT Connect, the 32nd annual scientific symposium of the Cardiovascular Research Foundation (CRF).

The ultra-low profile fixed-wire and rapid exchange DES systems used in the OPTIMIZE trial are designed to facilitate TR access and DS, potentially reducing the time and cost of PCI. The novel DES integrated delivery system (Slender IDS) combines a CoCr platform and bioresorbable amino acid-based (PEA) drug carrier eluting sirolimus mounted on a low-compliant balloon with an integrated 0.014" Asahi-Intecc guide wire. The same DES used with Slender IDS was also used with a rapid-exchange system (Direct RX) in the study.

OPTIMIZE was a prospective, single-blind, randomized, international, multi-center IDE trial comparing the new stent to existing drug-eluting stents (Xience or Promus EES) in 1,639 subjects with ischemic heart disease with 3 or less de novo stenotic lesions (34mm or less in length) in 2 or less native coronary arteries with RVD 2.25 mm—4.00 mm amenable to PCI. The primary endpoint, target lesion failure (TLF), was powered for noninferiority at 12 months.

From January 2018 to June 2019, 1,639 subjects (72% male, 30% diabetic, 57% acute coronary syndrome, mean age 65.4 years) with 1,988 lesions (74% Type B2/C, 36% moderate-severely calcified, 20% vessel angulation > 45°, mean stenosis 64%, lesion length 14.6 mm, RVD 2.78 mm) were 1:1 randomized at 74 investigative sites in the US (57%), Europe (34%) and Japan (9%).

At 12 months the rate of TLF was 10.3% in the Svelte group and 9.5% in the Xience/Promus group (difference = 0.8% [-inf, 3.8%] PNI = 0.034 which was above the prespecified 0.025 threshold for non-inferiority). No differences were observed between the two groups for the secondary endpoint, 12-month components of TLF: clinically indicated target lesion revascularization (TLR): 1.52% vs. 1.93%, p=0.57; cardiac death: 0.25% vs. 0.26%, p=1.00; TVMI: 9.31% vs. 8.22%, p=0.48.

"Based on the prespecified study statistical analysis plan, Svelte DES did not quite meet the threshold for non-inferiority using the prespecified absolute non-inferiority margin," said lead investigator Dean J. Kereiakes, MD. Dr. Kereiakes is Medical Director, The Christ Hospital Heart and Vascular Center, Medical Director, The Christ Hospital Research Institute and Professor of Clinical Medicine, The Ohio State University.

"However, independent analyses of OPTIMIZE results using either a comparable relative non-inferiority margin with the protocol definition of MI or

the SCAI definition of MI clearly demonstrate non-inferiority of Svelte DES to Xience/Promus. The high TVMI rates observed in both treatment groups was due to the use of high-sensitivity troponin biomarkers in 25% of OPTIMIZE subjects. High TVMI rates drove the higher than expected TLF rates which effectively underpowered the study. Other clinical outcomes were excellent, with very low rates of TLR and stent thrombosis. Standardization of IDE study definitions and biomarkers used in assessment of TVMI is urgently needed as evolving changes in biomarker selection will impact the size and integrity of future pivotal DES trials."

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