Novel Design Changes in DES Not Necessarily Better Until Proven So

Written by Rita Buckley

A drug-eluting stent (DES) is a "combination product" in which changes to one component may affect others; small alterations to strut thickness and geometry, polymer, drug, dose, and kinetics may result in big outcome changes, for better or worse. Mitchell W. Krucoff, MD, Duke University Medical Center Durham, North Carolina, USA, discussed the many factors involved in the development and deployment of novel stents.

According to Dr. Krucoff, the respective a priori and corollary rules for assessing breakthrough medical device technology are 1) the first generation is the worst generation; 2) just because a product is new does not prove that it is better; and 3) expect the unexpected.

For example, Daemen et al. [*Lancet* 2007] found that late stent thrombosis (beyond 30 days) was encountered at a steady rate over time, with no evidence of diminution up to 3 years of follow-up. Early and late stent thromboses were observed with sirolimus-eluting stents (SES; n=3823) and with paclitaxel-eluting stents (PES; n=4323). Acute coronary syndrome at presentation and diabetes were independent predictors of stent thrombosis.

The US Food and Drug Administration considers DES combination products with 3 components: stent platform design (ie, material composition, strut thickness, surface area, durability), polymer (ie, biocompatibility, consistency, durability), and drug (ie, dose, kinetics).

Ormiston et al. [*JACC Cardiovasc Interv* 2011] undertook standardized bench-top compression and elongation testing to assess the longitudinal strength of contemporary stents. They found that a stent design change ensuring 3 connectors, especially at the proximal end of a stent, should increase longitudinal integrity but perhaps at the expense of stent flexibility.

Although the polymer used in manufacturing has also been an issue, advances in polymer engineering now enable the production of DESs that are biocompatible, bioabsorbable, and have zero polymer. The Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects with De Novo Native Coronary Artery Lesions clinical trial [SPIRIT] evaluated the safety and efficacy of an everolimus stent versus a paclitaxel-eluting coronary stent. The primary outcome was ischemia-driven target lesion failure at 1 year. The authors found that the everolimus-eluting stent led to reduced rates of target lesion failure at 1 year compared with the PES. Results were consistent in all patients except those with diabetes [Stone GW et al. *N Engl J Med* 2010].

Krucoff and colleagues [*JACC Cardiovasc Interv* 2011] found similar results in the XIENCE V Everolimus Eluting Coronary Stent System Condition-of-Approval Post-Market [XIENCE V USA] study. There was a notable absence of stent thrombosis (ST) after dual antiplatelet therapy interruption beyond 6 months in standard- and high-risk patients.

Based on these outcomes and other factors of importance in the design and development of DES, Dr. Krucoff concluded that engineering and design objectives are the key to better and safer DES; design endpoints range from procedural (deliverability) to biological (late loss, endothelialization) to clinical (angina, myocardial infarction, ST, death); design targets include novel aspects of stent platform, drug, and drug-delivery systems; and achieving novel design changes is not enough to claim noninferiority or superiority until clinical data confirm better outcomes.