Third-Generation ZES Matches EES in Efficacy and Safety, Without Evidence of Longitudinal Deformation in an All-Comer Population

Written by Nicola Parry

Clemens von Birgelen, MD, PhD, Thoraxcentrum Twente, Enschede, The Netherlands, presented 1-year data from the Durable Polymer-Based Stent Challenge of Promus Element Versus Resolute Integrity in an All Comers Population [DUTCH PEERS (TWENTE II); von Birgelen C et al. *Lancet* 2013 (epublished ahead of print)] study. The results demonstrated comparable clinical outcomes with zotarolimus-eluting stents (ZES) and everolimus-eluting stents (EES); both are third-generation, permanent, polymer-based, drug-eluting stents (DES). There was no significant difference in efficacy and safety between the two stents, and longitudinal stent deformation was only seen in the EES group.

The introduction of DES has constituted a major breakthrough in the field of interventional cardiology, markedly reducing the incidence of restenosis and morbidity [Karjalainen P, Nammas W. *Minerva Cardioangiol* 2011]. Newer third-generation stent technology has been developed in an attempt to further enhance DES performance, and these durable-polymer-based DES aim to meet the need for more flexible and highly deliverable devices for the treatment of more challenging coronary lesions and vascular anatomy. While the coatings of third-generation stents remain similar to those of second-generation DES, changes in the material and design of their more flexible bare-metal platforms have the potential to reduce longitudinal stent stability.

To date, however, long-term data to compare the efficacy of currently available third-generation DES are still lacking [Akin I et al. *Herz* 2011].

DUTCH PEERS is a prospective, single-blinded, randomized, controlled trial in patients requiring percutaneous coronary intervention (PCI) with DES placement. The study was performed in 4 PCI centers in The Netherlands, and was designed to evaluate clinical outcomes after stenting with two third-generation DES that are frequently used clinically, but that had not previously been compared. It is the first all-comer trial with the platinum-chromium EES to be undertaken in a predominantly Caucasian population. A total of 20.4% of patients presented with a STEMI (requiring primary PCI), overall 58.6% had acute coronary syndromes, and 59.0% were treated for at lesions in small vessels.

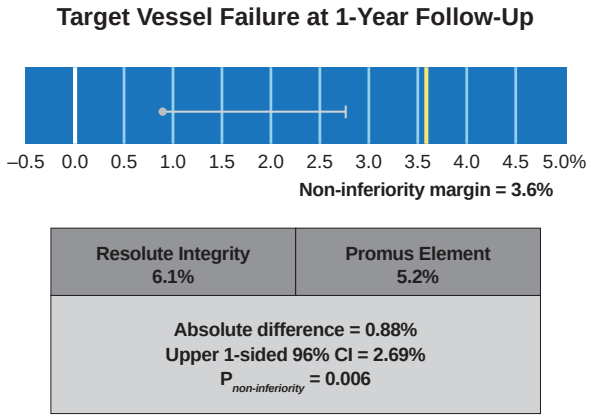
Patients were eligible to be included if they were aged ≥18 years, were able to provide informed consent, and had coronary artery disease and lesions eligible for DES treatment. There were no restrictions on clinical presentation or extent of coronary artery disease. Exclusion criteria included participation in another randomized clinical trial prior to reaching the primary endpoint; planned surgery within 6 months of PCI unless dual antiplatelet therapy was able to be continued during the surgery; pregnancy; life expectancy <1 year; and P2Y12 receptor antagonist intolerance, resulting in inability to adhere to dual antiplatelet therapy, or intolerance to heparin, aspirin, or components of the DES.

The primary endpoint was target vessel failure (TVF) at 1 year and was defined as the composite of cardiac death, target vessel-related myocardial infarction, or target vessel revascularization.

A total of 1811 patients with 2371 target lesions were enrolled in the study and randomized to either treatment with third-generation cobalt-chromium ZES (n=906; 1205 lesions), or platinum-chromium EES (n=905; 1166 lesions).

At 1 year, there was no statistically significant difference between the ZES and EES groups on the primary composite endpoint of TVF (6.1% vs 5.2%; p=0.42; p=0.006 for noninferiority; Figure 1), or in its individual components. Similarly, there was no significant difference between the two groups in the incidence of definite or probable stent thrombosis (0.6% vs 0.9%; p=0.4). There were no definite stent thromboses recorded at 3 months post implantation in either group. Longitudinal stent deformation was seen only in the EES group (1.0%; p=0.002) but not related to any adverse clinical events.

Figure 1. Primary Endpoint Data for DUTCH PEERS (TWENTE II)



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Prof. von Birgelen concluded that data from the DUTCH PEERS study demonstrate that treatment with either third-generation ZES or EES result in similar, clinical outcomes at 1 year.

Prolonged DAPT Is Unnecessary Post-Stenting in Patients Who Are Event-Free at 1Year

Written by **Nicola Parry**

Gilles Montalescot, MD, PhD,Institut de Cardiologie, Pitié-Salpêtrière University Hospital, Paris, France, presented data from the Assessment by a Double Randomization of a Conventional Antiplatelet Strategy Versus a Monitoring-Guided Strategy for Drug-Eluting Stent Implantation and of Treatment Interruption Versus Continuation One Year After Stenting trial [ARCTIC-INTERRUPTION; NCT00827411], demonstrating that patients who do not experience a major cardiac event within 1 year of drug-eluting stent (DES) implantation may not require long-term dual antiplatelet therapy (DAPT).

Uncertainty regarding the optimal duration of DAPT poses a challenge in the management of patients following DES implantation [Kandzari DE et al. *JACC Cardiol Intv* 2009]. International guidelines differ, and in North America, long-term DAPT, for at least 12 months, is recommended in these patients [Feres F et al. *JAMA* 2013; Levine GN et al. *Circulation* 2011], while European guidelines recommend at least 6 months DAPT [Wijns W et al. *Eur Heart J* 2010]. To date, DAPT extended beyond 12 months has been considered to favor clinical outcomes in selected patients [Feres F et al. *JAMA* 2013; Levine GN et al. *Circulation* 2011; Wijns W et al. *Eur Heart J* 2010]. However, evaluation of pooled data from several randomized studies has suggested that extended DAPT offers no ischemic benefit to patients, and appears to increase the incidence of major bleeding events [Cassesse S et al. *Eur Heart J* 2012].

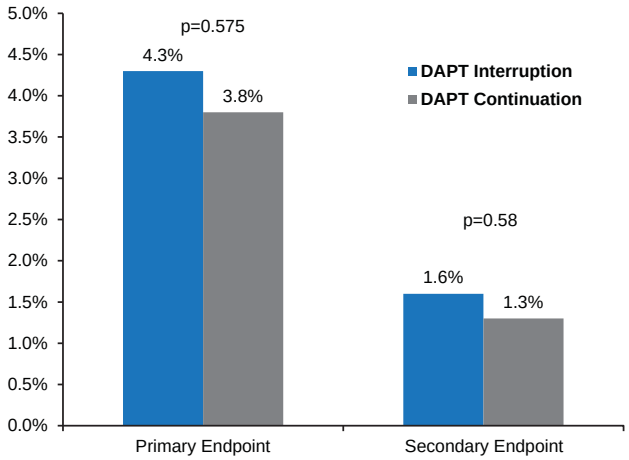
ARCTIC-INTERRUPTION was a prospective, randomized trial that was designed to compare the safety and clinical impact of 12 months versus 18 to 30 months of DAPT after percutaneous coronary intervention (PCI). The trial was an extension of the original ARCTIC trial, which demonstrated that monitoring platelet function in patients (n=2440) receiving antiplatelet therapy did not improve clinical outcomes [Collet JP et al. *N Engl J Med* 2012].

Randomization occurred at the end of the first year of follow-up after stenting. The primary endpoint of the ARCTIC-INTERRUPTION trial was the composite of death, myocardial infarction (MI), stent thrombosis, stroke, or urgent revascularization after 1 year. The major secondary endpoint was stent thrombosis or any urgent revascularization.

A total of 1259 patients from the original ARCTIC trial who were free of major events within a year after coronary stenting were included in the study, and re-randomized to either interruption of the DAPT regimen with a switch to single antiplatelet therapy (n=624), or continued DAPT for up to an additional year (n=635). Patients were excluded if they had any primary efficacy or safety endpoints during the first 12 months of follow-up; any new revascularization requiring prolonged DAPT; contraindication to aspirin continuation; or physician or patient decision not to stop thienopyridine at 1 year.

There was no statistically significant difference between the DAPT interruption and DAPT continuation groups with respect to occurrence of the primary endpoint up to 18 months after randomization (4.3% vs 3.8%; HR, 1.17; 95% CI, 0.68 to 2.03; p=0.575), or secondary endpoint (1.6% vs 1.3%; HR, 1.30; 95% CI, 0.51 to 3.30; p=0.58; Figure 1).

Figure 1. Primary and Secondary Endpoints



DAPT=dual antiplatelet therapy.

Major bleeding events occurred more frequently in the DAPT continuation versus the DAPT interruption group, although this difference was not statistically significant (1.1% vs 0.2%; HR, 0.15; 95% CI, 0.02 to 1.20; p=0.073). A significant difference was found, however, with respect to major or minor bleeding events (1.9% vs 0.5%; HR, 0.26; 95% CI, 0.07 to 0.91; p=0.035).

Prof. Montalescot concluded that in patients who have not experienced a major adverse event within the first year after stent implantation, prolonged continuation of DAPT beyond this time does not provide additional clinical benefit in protecting against ischemia. Additionally, longer-term DAPT may increase the risk of bleeding events.