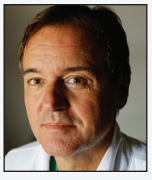
Clinical Data for Stenting High-Risk Patients Requiring Short DAPT

Discussing the clinical benefits of the COBRA PzF NanoCoated Coronary Stent (NCS).

WITH GILLES MONTALESCOT, MD, PhD; AXEL de LABRIOLLE, MD, PhD; AND DONALD CUTLIP, MD



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Complications from bleeding after percutaneous coronary intervention (PCI) occur more frequently than myocardial infarctions and have a greater impact on mortality.[1] Patients at high risk of bleeding and thrombosis have historically been a challenging population to treat due to concerns with the safety of drug-eluting stents (DES) with short dual antiplatelet therapy (DAPT) and the efficacy of bare-metal stents due to higher rates of restenosis.

The eCOBRA study is a prospective, multicenter, all-comers study composed of 1,026 patients across 17 centers designed to evaluate the safety and effectiveness of the COBRA PzF NanoCoated Stent (NCS); (CeloNova BioSciences, Inc.; Figure 1), a new category of durable polymer-coated, non-DES, in a real-world setting of highly complex patients, such as those at high risk of bleeding and thrombosis who are not indicated for DES and require very short DAPT. The clinical trial demonstrated

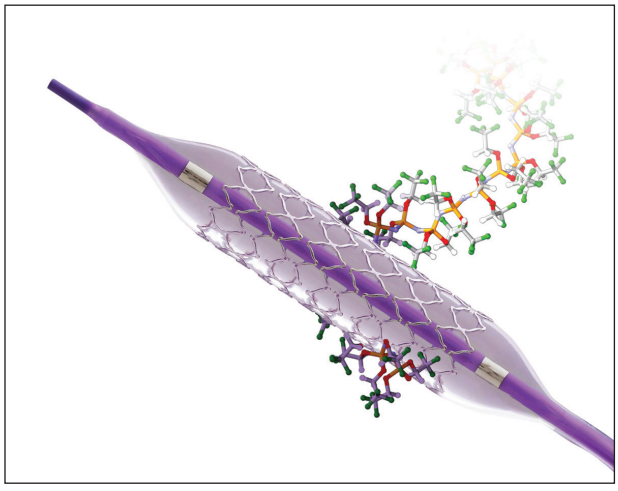

Figure 1. The COBRA PzF NCS is a new category of durable polymer-coated, non-DES.

positive outcomes at 1 year with a 4.3% rate of target lesion revascularization (TLR), a 0.3% rate of late stent thrombosis, and an 8.6% rate of major adverse cardiovascular events (MACE).

The eCOBRA trial expands upon the PzF SHIELD IDE trial's exceptional results that demonstrated COBRA PzF NCS is safe and effective for patients who may benefit from a minimum of 1-month DAPT in accordance with current guidelines.[2,3] COBRA PzF NCS is now being studied with even shorter, 14-day DAPT in the COBRA REDUCE IDE trial in patients at high risk of bleeding.*

What is the main objective and study design of the eCOBRA study?

Dr. Montalescot: eCOBRA is a prospective, multicenter, single-arm study of the novel COBRA PzF NCS in patients requiring short DAPT because of their high bleeding risk. All patients underwent treatment of de novo lesions in native coronary vessels, saphenous vein graft, and/or arterial bypass conduits with the COBRA PzF NanoCoated Coronary Stent System. They were patients at high bleeding risk or considered inappropriate to receive a DES. In the absence of a control group, indirect comparisons confirm excellent results shown by small registries and the PzF SHIELD study conducted under IDE. With similar indirect comparisons, the MACE, stent thrombosis, and death rates compare favorably with other studies, such as LEADERS FREE.[4]

How well was the eCOBRA study executed and what are the results?

Dr. de Labriolle: eCOBRA is the first very large multicenter registry led in France from 2016 to 2017 that was open to all comers, including very complex patients. The 30-day results were presented at EuroPCR in 2017 and the 1-year results were presented this past May at EuroPCR in 2018.

The most important particularity of this registry was the severity of included patients—as much on clinical presentation and hemorrhagic risk as the severity of the lesions. This very high-risk population was a good test of performance for COBRA PzF NCS. The median patient age was 76 years, atrial fibrillation was present in 23% of patients, 56% of patients received PCI for acute coronary syndrome, and 30% patients had very complex lesions (eg, B2/C ACC/AHA classification).

When we look at the endpoints, we observe solid results with a total MACE rate of 8.6%, a low rate of clinically driven TLR (4.3%), a very low rate of 1-year definite/probable stent thrombosis (1.2%), and a particularly low rate of late stent thrombosis (0.3%).

These observed results appeared to be better than those observed in the LEADERS FREE study,[4] which has so far been the point of reference in this population of complex patients.

Do these results change your approach to treating high-risk patients?

Dr. Montalescot: The eCOBRA study is a solid study with compelling results from real-world practice. Evaluations of COBRA PzF NCS as a next-generation stent compared to current DES are also underway in the COBRA REDUCE 14-day DAPT randomized study, which aims to further evaluate COBRA PzF NCS as a good option for those high-risk patients requiring short DAPT.

Dr. de Labriolle: eCOBRA brings preliminary evidence in safety and efficacy for COBRA PzF NCS to be proposed for complex PCI in complex patients and particularly in patients requiring short DAPT. These data will soon be confirmed by the ongoing COBRA REDUCE international multicenter randomized study, which compares COBRA PzF NCS to standard DES in these clinical scenarios. In our center, we use COBRA PzF NCS as first-line treatment in all patients with high hemorrhagic risk or those who need short DAPT.

Dr. Cutlip: eCOBRA demonstrates excellent results in a population selected on the basis of absence of DES indication. As the results indicate, this included mostly those patients at higher risk for bleeding with patient characteristics similar in complexity to other trials of patients with high bleeding risk. In particular, the high complexity is reflected by a mean age over 76 years and more than 50% of included patients had acute coronary

syndrome. On this background, the low risk for stent thrombosis coupled with a low risk for TLR are reassuring and suggest that COBRA PzF NCS can be considered as a viable option among patients at high bleeding risk or who have other limitations to prolonged DAPT.

How does eCOBRA fit into the broader COBRA PzF NCS clinical program?

Dr. Cutlip: The eCOBRA study can be added to other trials that have included several studies of an earlier-generation PzF stent, the early unselected experience of COBRA PzF NCS, and the pivotal COBRA PzF SHIELD trial that compared outcomes with a historical performance goal.[5] These studies have been consistent in confirming both the low thrombosis and low restenosis potential demonstrated during extensive preclinical evaluation. With consistently low clinically driven TLR rates of approximately 5% and very low definite or probable stent thrombosis rates even in the complex patient population enrolled in eCOBRA, the device combines excellent safety and effectiveness.[6,7] In the studies thus far, COBRA PzF NCS appears to rival the best results of DES among high bleeding risk patients. The results of the randomized COBRA REDUCE trial comparing COBRA PzF NCS and 14 days of DAPT with an everolimus-eluting stent and 3 to 6 months of DAPT will help determine more precisely how COBRA PzF NCS and very short-term DAPT fit into the management of this important group of patients.

What do you see for the future of COBRA PzF NCS?

Dr. Montalescot: Considering that high bleeding risk and high ischemic risk are often present in the same patients, COBRA PzF NCS, with the current information we have, appears as a good stent to allow reduction of DAPT duration, which is being evaluated in the ongoing COBRA REDUCE trial.

Dr. de Labriolle: The next step is to demonstrate that in less-high-risk patients, COBRA PzF NCS is as efficient as the standard DES. Given the results concerning vessel healing, COBRA PzF NCS should also be tested with single antiplatelet therapy—much less than what is currently recommended.

Dr. Cutlip: Right now, there are compelling data to support the use of COBRA PzF NCS in patients at high bleeding risk. Potential for expanding this role will depend greatly on the results of the ongoing COBRA REDUCE trial. If very short-term DAPT is deemed safe and if clinical restenosis rates compare favorably with best-of-class DES, then COBRA PzF NCS could be the preferred option among patients with high bleeding risk. This may spark further studies to assess short-term single antiplatelet therapy and provide an even safer option. ■

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*For more information about the COBRA REDUCE IDE trial, please visit: clinicaltrials.gov/ct2/show/NCT02594501.

Indications for Use: The COBRA PzF NanoCoated Coronary Stent System is indicated for improving coronary luminal diameter in patients, including patients with diabetes mellitus, with symptomatic ischemic heart disease due to de novo lesions in native coronary arteries. The COBRA PzF NanoCoated stent is intended for use in patients eligible for percutaneous transluminal coronary angioplasty (PTCA) with reference vessel diameter (RVD) of 2.5-4.0 mm and lesion length of ≤ 24mm.

Visit www.celonova.com/cobra-pzf-nanocoated-stent/precautions for IMPORTANT SAFETY INFORMATION.

Contraindications: The COBRA PzF NanoCoated Coronary Stent System is contraindicated for use in patients with known sensitivity to L605 cobalt-chromium alloy (including its major elemental constituents cobalt, chromium, tungsten, and/or nickel). Contraindication to coronary artery stenting: Patients with lesions that may prevent complete inflation of an angioplasty balloon, proper placement of the delivery device or stent deployment, Patients are unable to receive recommended anti-platelet and/or anti-coagulant therapy. Known severe reaction to contrast agents that cannot be adequately pre-medicated prior to the COBRA PzF NanoCoated Coronary Stent System placement procedure.

Warnings/Precautions: Use of this device carries the associated risks of stent thrombosis, vascular complications, and bleeding events. Judicious patient selection and administration of appropriate anticoagulant and antiplatelet therapy are necessary to reduce these risks. Compared to use within the specified Indications for Use, the use of COBRA PzF NanoCoated stents in patients and lesions outside the labeled indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death.

See the Instructions for Use for complete information regarding the procedure, indications for use, contraindications, warnings, precautions, and potential adverse events. Rx Only