

## New drug-eluting stents: technological refinement continues



### *Nuevos stents farmacoactivos: el refinamiento tecnológico continúa*

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The arrival of drug-eluting stents (DES) nearly 2 decades ago ignited a revolution in the field of interventional cardiology. The addition of antiproliferative drugs to the stent platform reduced the rate of in-stent restenosis significantly and increased the number of patients that, to this date, have benefited from percutaneous revascularization.<sup>1,2</sup> However, its Achilles tendon was initially the higher rate of late stent thrombosis involved. The permanent polymer used in the first generation of DES induced inflammatory and hypersensitivity reactions that delayed endothelization. A health alert followed<sup>3</sup> that made the medical community recommend extended courses of dual antiplatelet therapy and put into question the convenience of DES. Beyond the increased rate of stent thrombosis, the first-generation of this type of stents had additional limitations: they were stainless-steel platforms with up to 140 µm thick struts, worse stent navigability, and fewer crossing capabilities. Also, the stent maximum expansion was limited (3.5 mm in the Cypher stent, Cordis Corp.), which occasionally prevented treating left main coronary artery lesions. With the passing of time, this stent technology has been refined to a point that there has been a major overhaul in its 3 main components: platform, polymer, and anti-proliferative drug.

The changes made to the stent platform have been the development of more biocompatible alloys that have reduced strut thickness significantly and, consequently, improved stent navigability. Additionally, radial strength has been preserved to prevent recoil (table 1). Most of the stents commonly used today consist of cobalt-chromium or platinum-chromium alloys. The open-cell design has won the battle over the closed-cell design because it reduces the number of inter-strut links, the degree of jailed side-branch while improving stent navigability and conformability. Also, the new generation of DES have wider overexpansion limits (4.5 mm to 6 mm), which allows us to treat left main coronary artery lesions by adapting the stent area to the corresponding luminal references without damage to the platform.

Polymers are the reservoir from which the drug is released in a controlled way towards the arterial wall. XIENCE (Abbott), and Resolute Onyx (Medtronic) stents include permanent polymers, but

with improved biocompatibility. The XIENCE polymer is highly fluorinated, which minimizes adhesion and platelet activation increasing the safety profile. The Onyx stent uses Biolinx that consists of a mixture of polymers with hydrophilic capabilities that make it biocompatible and hydrophobic for a prolonged and uniform drug release. However, despite the good results reported with the new permanent polymers, some companies have decided to develop bioresorbable polymers (SYNERGY [Boston Scientific], Orsiro [Biotronik], Ultimaster Tansei [Terumo] stents, etc.). The use of a bioresorbable polymer-based coating facilitates degradation after the drug complete release just leaving 1 bare-metal stent behind 3-4 months after implantation, which prevents the remaining polymer from participating in the immune response associated with stent thrombosis. The biodegradable polymer-based SYNERGY stent has shown a rate of stent thrombosis of 0% at the 6-month follow-up, and a rate of target lesion revascularization similar to the one observed with the permanent polymer-based Promus Element stent (Boston Scientific).<sup>4</sup> On the other hand, the biodegradable polymer-based Orsiro stent had a significantly lower rate of target lesion failure compared to the XIENCE stent with permanent polymer.<sup>5</sup> However, the XIENCE stent group had more and longer stents implanted, both factors associated with adverse events at follow-up.

Polymer-free stents stand as an alternative to biodegradable polymer-based stents. The most representative of the former is the BioFreedom (Biosensors). It consists of a stainless-steel platform with micropores that store biolimus for a 1-month release of the drug. The lack of a polymer may potentially allow to shorten the duration of the period on dual antiplatelet therapy down to 1 month, like with bare metal stents. In the LEADERS FREE trial,<sup>6</sup> the BioFreedom was compared to a bare metal stent in patients with high-risk of bleeding and a 1-month course of dual antiplatelet therapy. The outcomes proved that it was superior regarding the primary evaluation criteria for the safety and efficacy profile. Afterwards, almost every company has conducted or started safety and efficacy trials with 1-month courses of dual antiplatelet therapy (table 1).

Therefore, several advances have been made with new generation DES. The clinical impact associated with strut thickness reduction

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**Table 1.** Characteristics of drug-eluting stents

Stent	Platform	Polymer/ coating	Drug	Strut thickness ( $\mu\text{m}$ )	Maximum expansion (mm)	Studies with 1 month DAPT duration
XIENCE	Cobalt-chromium	Permanent/ circumferential	Everolimus	81	2.3-2.5 $\rightarrow$ 3.75 3.5-4 $\rightarrow$ 5.5	Xience 28 USA (NCT03815175)
SYNERGY	Platinum-chromium	Bioresorbible/ abluminal	Everolimus	74	2.25 $\rightarrow$ 3.5 3-3.5 $\rightarrow$ 4.25 4-5 $\rightarrow$ 5.75	SENIOR (NCT02099617)
Onyx	Nickel-platinum-chromium	Permanent/ circumferential	Zotarolimus	81	2.5-3 $\rightarrow$ 3.75 3.5-4 $\rightarrow$ 4.75 4.5-5 $\rightarrow$ 5.75	Onyx ONE (NCT03344653)
Orsiro	Cobalt-chromium	Bioresorbible/ circumferential	Sirolimus	60	2.5-3 $\rightarrow$ 3.5 3.5-4 $\rightarrow$ 4.5	Bioflow-DAPT (NCT04137510)
Ultimaster Tansei	Cobalt-chromium	Bioresorbible/ abluminal	Sirolimus	80	2.25-3 $\rightarrow$ 4.5 3.5-4 $\rightarrow$ 5.5	Master DAPT (NCT03023020)
BioFreedom	Stainless-steel	Polymer-free/ abluminal	Umirolimus	112	2.5-3 $\rightarrow$ 4.76 3.5-4 $\rightarrow$ 5.96	LEADERS FREE (NCT01623180)
Angiolite	Cobalt-chromium	Permanent/ circumferential	Sirolimus	75-85	2-2.5 $\rightarrow$ 4 2.75-3.5 $\rightarrow$ 5.25 4-4.5 $\rightarrow$ 6	–

DAPT, dual antiplatelet therapy.

or the selection of bioresorbable polymer-based stents vs permanent or polymer-free stents is still under discussion. However, these improvements have had significant repercussions in the stent navigability, overexpansion capabilities, and selection of duration for dual antiplatelet therapy. However, these stent properties highly demanded by interventional cardiologists should always be based on a robust set of trials that confirm the efficacy and safety profile of each stent. Currently, the Angiolite stent (iVascular) is in this stage. It has recently joined the family of DES. This stent is an ultra-thin strut (75  $\mu\text{m}$  to 85  $\mu\text{m}$ ) cobalt-chromium platform made from a biostable fluorinated polymer plus sirolimus as the antiproliferative drug. In the ANCHOR trial it showed an excellent degree of endothelialization on the optical coherence tomography,<sup>7</sup> with an 83% strut endothelial coverage at 3 months. Afterwards, the ANGIOLITE trial compared it to the standard DES and found a 0.04 mm late luminal loss vs the 0,08 mm of the XIENCE stent, as well as a low rate of events at the 2-year follow-up in both groups<sup>8</sup> (target lesion failure, 7.1% with the Angiolite vs 7.6% with the XIENCE). In an article published on *REC Interventional Cardiology*, Pérez de Prado et al.<sup>9</sup> presented a multicenter real-world registry of patients treated with the Angiolite stent. This registry could be considered the «moment of truth» for this stent. We should remember that the Absorb stent (Abbott) had excellent immediate results and at the 5-year follow-up<sup>10</sup> in the early trials. However, it showed a high rate of stent thrombosis when used in real-world patients. The ANCHOR registry included 646 patients with a 2-year clinical follow-up. A total of 30% of these patients were diabetics. ST-segment elevation myocardial infarction was the clinical presentation in almost 25% of these patients, and nearly 50% of them had multivessel disease. The rate of target vessel failure and the rate of stent thrombosis at the 2-year follow-up were 3.4%, and 0.9%, respectively. In this sense, the stent offers similar results to those obtained with state-of-the-art DES as the table of the supplementary data of the aforementioned article shows.<sup>9</sup> However, these promising results will need to be confirmed at the 5-year follow-up. The behavior of the stent in the most complex lesions like bifurcations or chronic total occlusions associated with worse clinical outcomes—underrepresented in the registry—also needs to be assessed.

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## CONFLICTS OF INTEREST

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## REFERENCES

- Moses JW, Leon MB, Popma JJ, et al.; SIRIUS Investigators. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med.* 2003;349:1315-1323.
- Stone GW, Ellis SG, Cox DA, et al.; TAXUS-IV Investigators. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med.* 2004;350:221-231.
- Camenzind E, Steg PG, Wijns W. Stent thrombosis late after implantation of first-generation drug-eluting stents: a cause for concern. *Circulation.* 2007;115:1440-1455.
- Meredith IT, Verheye S, Dubois CL, et al. Primary endpoint results of the EVOLVE trial: a randomized evaluation of a novel bioabsorbable polymer-coated, everolimus-eluting coronary stent. *J Am Coll Cardiol.* 2012;59:1362-1370.
- Kandzari DE, Mauri L, Koolen JJ, et al. Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a randomised trial. *Lancet.* 2017;390:1843-1852.
- Urban P, Meredith IT, Abizaid A, et al. Polymer-free drug-coated coronary stents in patients at high bleeding risk. *N Engl J Med.* 2015;373:2038-2047.
- Puri R, Otaegui I, Sabate M, et al. Three- and 6-month optical coherence tomographic surveillance following percutaneous coronary intervention with the Angiolite(R) drug-eluting stent: The ANCHOR study. *Catheter Cardiovasc Interv.* 2018;91:435-443.

8. Moreu J, Moreno-Gomez R, Perez de Prado A, et al. First-in-man randomised comparison of the Angiolite durable fluoroacrylate polymer-based sirolimus-eluting stent versus a durable fluoropolymer-based everolimus-eluting stent in patients with coronary artery disease: the ANGIOLITE trial. *EuroIntervention.* 2019;15:e1081-e1089.
9. Pérez de Prado A, Ocaranza-Sánchez R, Lozano Ruiz-Poveda F, et al. Real-world registry of the durable Angiolite fluoroacrylate polymer-based sirolimus-eluting stent: the EPIC02-RANGO study. *REC Interv Cardiol.* 2021. <https://doi.org/10.24875/RECICE.M21000223>.
10. Onuma Y, Dudek D, Thuesen L, et al. Five-Year Clinical and Functional Multislice Computed Tomography Angiographic Results After Coronary Implantation of the Fully Resorbable Polymeric Everolimus-Eluting Scaffold in Patients With De Novo Coronary Artery Disease: The ABSORB Cohort A Trial. *JACC Cardiovasc Interv.* 2013;6:999-1009.