A Review of the Ultrathin Orsiro Biodegradable Polymer Drug-eluting Stent in the Treatment of Coronary Artery Disease

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Drug-eluting stents (DES) have revolutionised the treatment of coronary artery disease (CAD) in patients undergoing percutaneous coronary intervention. In recent years, there has been a focus on a new generation of DES, such as biodegradable polymer DES (BP-DES). This novel stent platform was developed with the hope of eliminating the risk of very late stent thrombosis associated with the current gold-standard durable polymer DES (DP-DES). Ultrathin Orsiro BP-DES (Biotronik, Bülach, Switzerland) are based on a cobalt-chromium stent platform that is coated with a bioresorbable polymer coating containing sirolimus. These devices have one of the thinnest struts available in the current market and have the theoretical benefit of reducing a chronic inflammatory response in the vessel wall. In 2019, the United States Food and Drug Administration (FDA) approved the use of Orsiro BP-DES in patients with CAD based on promising results in recent landmark trials, such as BIOFLOW V and BIOSTEMI. The aim of the present review article was to discuss the history of stent technology and the continued opportunities for improvements, focusing on the potential benefits of Orsiro BP-DES.

Keywords

Biodegradable polymer, coronary artery disease, drug-eluting stents, Orsiro

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Coronary artery disease (CAD) is a major global cause of death attributing to nearly 9 million deaths worldwide in 2016.[1] The introduction of percutaneous coronary intervention (PCI) has revolutionised the treatment of CAD in current clinical practice, and advances in coronary stent technology have continued to deliver improved outcomes. In recent years, there has been a focus on a new generation of drug-eluting stents (DES), such as biodegradable polymer DES (BP-DES). This novel stent platform utilises a bioresorbable polymer coating that provides controlled release of an anti-proliferative drug.

A number of innovations in stent design have been made to address the risk of very late stent thrombosis (ST) associated with the current gold-standard durable polymer DES (DP-DES). In 2019, the US Food and Drug Administration (FDA) approved the use of ultrathin Orsiro BP-DES (Biotronik, Bülach, Switzerland) in patients with CAD.[2] New-generation DES have demonstrated promising results in landmark trials. The aim of this review article was to discuss the history of stent technology and the continued opportunities for improvements, focusing on the potential benefits of Orsiro BP-DES.

Percutaneous transluminal coronary angioplasty

Coronary stent technology has made remarkable progress over the last few decades in terms of stent design, structure, and component materials.[3] Percutaneous transluminal coronary angioplasty (PTCA) was first performed in 1977 by Grüntzig et al.[4] As a minimally invasive procedure, PTCA offers an alternative revascularisation strategy to coronary artery bypass grafting, especially for patients deemed unsuitable for surgery. However, during PTCA, balloon dilation causes atherosclerotic plaque disruption and endothelial denudation, which provoke vascular injury and inflammation.[5] This mechanical trauma also induces various processes, such as elastic recoil, intimal dissection, and neointimal hyperplasia.[6] These factors contribute to abrupt vessel closure and restenosis, which are limitations of PTCA.[7] Abrupt vessel closure refers to sudden coronary occlusion after PCI leading to myocardial infarction (MI). The incidence of abrupt vessel closure within 24 hours of PTCA was reported to be 8%.[8] Restenosis is defined as >50% reduction in lumen diameter after PCI.[9] The incidence of restenosis within 6 months of PTCA was reported to be 40%.[10]

Bare metal stents

Bare metal stents (BMS) were developed to address the limitations of PTCA. These devices are a stainless steel mesh tube that is delivered and expanded by a balloon-tipped catheter to optimise the lumen of the diseased vessel.[11] In current clinical practice, the majority of PCI procedures involve both angioplasty and stent placement. BMS implantation was first performed in 1986 by Sigwart et al.[12] The stent acts as a scaffold that prevents abrupt vessel closure and

restenosis by tacking intimal dissection flaps against the vessel wall and maintaining the widened lumen diameter.[13] Intravascular ultrasound was first introduced in the 1980s, and is routinely used in high-pressure balloon dilation to enhance stent expansion and strut apposition to the vessel wall.[14] Optical coherence tomography is an emerging imaging modality that can be applied as a periprocedural tool for stent planning, improving lumen assessment and plaque characterisation compared to intravascular ultrasound.[15] In current clinical practice, the use of intravascular imaging has been a major determinant in optimising stent expansion and placement.

In 1994, the FDA approved the use of BMS in patients with CAD.[16] The BENESTENT trial found that BMS had a significantly reduced rate of restenosis at 7 months compared with PTCA (22% versus 32%; p=0.02).[17] However, BMS were hindered by the risk of in-stent restenosis (ISR). During BMS implantation, stent expansion and strut apposition to the vessel wall provoke vascular injury and inflammation.[18] This mechanical trauma leads to neointimal hyperplasia and gradual narrowing of the lumen.[19] The incidence of ISR was reported to range from 17% to 41%.[20]

First-generation durable polymer drug-eluting stents

DP-DES were introduced to overcome the risk of ISR associated with BMS. These devices are based on a stainless steel stent platform that is coated with a permanent polymer containing an anti-proliferative drug.[21] The permanent polymer coating provides controlled release of the anti-proliferative drug over 4–6 weeks following DP-DES implantation, to inhibit neointimal hyperplasia and theoretically eliminate the risk of ISR associated with BMS.[22] DP-DES implantation was first performed in 1999 by Sousa et al.[23] First-generation DP-DES release sirolimus or paclitaxel, both of which are effective agents for modifying intracellular signalling to prevent neointimal hyperplasia.[24] Sirolimus is an immunosuppressive macrolide extracted from the bacterium *Streptococcus hygroscopicus* that prevents vascular smooth muscle cell proliferation by inhibiting mammalian target of rapamycin (mTOR) and arresting the cell cycle progression from G1 to S phase.[25] Paclitaxel is an antineoplastic drug extracted from the yew *Taxus brevifolia*. It prevents vascular smooth muscle cell proliferation by stabilising microtubules and arresting the cell cycle progression from G2 to M phase.[26] The RAVEL trial found that sirolimus-eluting stents (SES) had a significantly reduced rate of ISR at 6 months compared with BMS (0% versus 26.6%; p<0.001).[27] Similarly, the TAXUS I trial found that paclitaxel-eluting stents (PES) had significantly reduced in-stent late lumen loss at 12 months compared with BMS (0.36 ± 0.48 versus 0.71 ± 0.48 mm; p<0.01).[28] In-stent late lumen loss is defined as the difference in minimum lumen diameter within the stented segment immediately after PCI and at a specified follow-up period.[29] This angiographic measurement is used as a surrogate marker to estimate the risk of ISR.[30] The FDA approved the use of SES and PES in 2003 and 2004, respectively.[31]

Stent thrombosis

Despite resolving the limitations of BMS, first-generation DP-DES were impeded by the risk of ST. This adverse event can be classified according to the probability of event. According to the Academic Research Consortium,[32] definite ST is defined by either angiographic or pathological evidence of ST, probable ST is defined as either any unexplained death within 30 days of stent placement or any MI within the territory of implanted stent, and possible ST is defined as any unexplained death beyond 30 days. ST can also be classified according to the timing of event following stent placement. Acute ST occurs within 24 hours, subacute ST occurs between 1 and 30 days, late ST occurs beyond 30 days, and very late ST occurs beyond 12 months.[33]

The mechanism of ST is attributed to the permanent polymer coating that triggers a chronic inflammatory response in the vessel wall involving incomplete re-endothelialisation, neoatherosclerosis, and hypersensitivity reaction.[34,35] Sirolimus and paclitaxel in first-generation DP-DES are also toxic agents that potentiate the expression of tissue factor in endothelial cells and form a pro-thrombogenic environment leading to ST.[36] A challenge faced by novel stent platforms is the development of less toxic anti-proliferative drugs that provide an adequate balance between the inhibition of neointimal hyperplasia and the stimulation of early re-endothelialisation. There have been concerns about the safety profile of DP-DES, with the risks of late and very late ST. A pooled analysis of 1,748 patients found that there was a significantly increased rate of very late ST at 4 years for SES (0.6% versus 0%; p=0.025) and PES (0.7% versus 0.2%; p=0.028) compared with BMS.[37] The median timing of very late ST for SES and PES was reported to be 15.5 months and 18.0 months, respectively.[38]

Second-generation durable polymer drug-eluting stents

Second-generation DP-DES were developed to address the risk of very late ST associated with first-generation SES and PES. These devices are based on a similar structure to the preceding generation, but utilise more biocompatible polymer coatings, less toxic anti-proliferative drugs, and thinner metal alloy stent (cobalt-chromium or platinum-chromium) platforms.[39] Second-generation DP-DES release everolimus or zotarolimus, both of which are sirolimus analogues with shorter half-lives and fewer collateral effects.[40] The COMPARE trial found that everolimus-eluting stents (EES) had a significantly reduced rate of definite or probable ST at 5 years compared with PES (3.1% versus 5.9%; p=0.005).[41] Similarly, the ENDEAVOR IV trial found that zotarolimus-eluting stents (ZES) had a significantly reduced rate of very late ST at 5 years compared with PES (0.4% versus 1.8%; p=0.012).[42] The FDA approved the use of EES and ZES in patients with CAD in 2008 and 2012, respectively.[43] Second-generation DP-DES have largely replaced the preceding generation of devices, and are recognised as the current gold standard for PCI.[44] However, the issue of very late ST persisted in second-generation DP-DES. The incidence of very late ST over 5 years for EES and ZES was reported to be 1.5% and 1.3%, respectively.[45] Despite the use of more biocompatible materials, the permanent polymer coating in second-generation DP-DES remains a driving factor for very late ST.

Biodegradable polymer drug-eluting stents

The ongoing issue of very late ST associated with DP-DES has led to the advent of BP-DES. These new-generation DES are based on a metallic stent platform that is coated with a biodegradable polymer releasing an anti-proliferative drug.[46] The degradation of the polymer coating removes the potential stimulus for a chronic inflammatory response in the vessel wall, and theoretically eliminates the risk of very late ST associated with DP-DES. The polymer coating of BP-DES dissolves over time following stent placement, during which there is controlled release of the anti-proliferative drug.[47] The metallic stent platform remains in the vessel once the polymer coating has completely degraded. BP-DES release everolimus, sirolimus, or biolimus. Biolimus is a highly lipophilic sirolimus analogue that easily crosses the cell membrane to achieve rapid onset of action and minimal collateral effects.[48] In 2019, the FDA approved the use of ultrathin Orsiro BP-DES in patients with CAD, based on promising results in recent landmark trials.[2] *Table 1* summarises the characteristics of current DES.

Table 1: Characteristics of current drug-eluting stents

Stent	Manufacturer	Drug	Platform	Strut thickness (µm)
Second-generation DP-DES				
Xience	Abbott Vascular	Everolimus	CoCr	81
Resolute Integrity	Medtronic	Zotarolimus	CoCr	91
BP-DES				
Orsiro	Biotronik	Sirolimus	CoCr	60–80
Synergy	Boston Scientific	Everolimus	PtCr	79–81
Nobori	Terumo	Biolimus	SS	120

BP-DES = biodegradable polymer drug-eluting stents; CoCr = cobalt-chromium; DP-DES = durable polymer drug-eluting stents; PtCr = platinum-chromium; SS = stainless steel.

Strut thickness

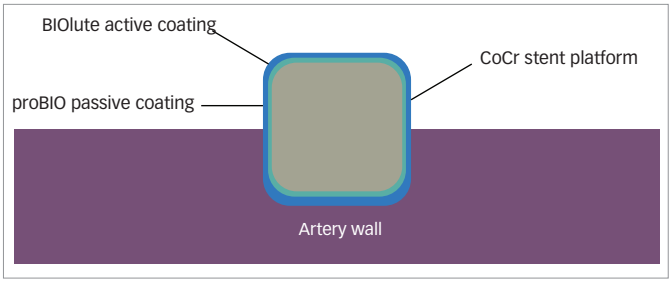
The importance of strut thickness to the clinical performance of DES has been demonstrated in several studies. An *ex vivo* study involving flow loops showed that thick-strut (162 µm) stents had 1.5-fold increase in thrombogenicity at 3 days compared with thin-strut (81 µm) stents (p<0.001).[49] An animal study involving rabbit denudation models showed that thin-strut (81 µm) stents had significantly increased strut tissue coverage at 14 days compared with thick-strut (132 µm) stents (77 ± 6% versus 95 ± 4%; p=0.001).[50] The thinner struts promote early re-endothelialisation and arterial healing due to the smaller area requiring neointimal tissue coverage.[51] The ISAR-STEREO trial found that thin-strut (50 µm) stents had significantly reduced rates of ISR at 6 months compared with thick-strut (140 µm) stents (15.0% versus 25.8%; p=0.003).[52] The thinner struts have less traumatic effect resulting in reduced vascular injury, inflammation and disruption of local blood flow.[51] The thinner struts also enable greater flexibility for stent delivery through calcified or tortuous vessels.[53]

Orsiro BP-DES have one of the thinnest struts available in the current market, with a strut thickness of either 60 µm for the 2.25–3.00 mm stent platform or 80 µm for the 3.50–4.00 mm stent platform.[54] Nobori® BP-DES (Terumo, Tokyo, Japan) are similar devices, with a strut thickness of 120 µm.[55] The SORT OUT VII trial found that Orsiro BP-DES had a significantly reduced risk of definite ST at 12 months compared with Nobori BP-DES (0.4% versus 1.2%; p=0.03).[56] The investigators suggested that thinner struts have the potential to reduce thrombogenicity and thrombus mobilisation.

Dual antiplatelet therapy

The introduction of dual antiplatelet therapy (DAPT) led to a reduced risk of ST associated with DES. DAPT has been adopted as the routine antithrombotic regimen following stent placement, and consists of aspirin plus adenosine diphosphate ($P2Y_{12}$) receptor inhibitor.[57] According to the latest American College of Cardiology/American Heart Association guidelines, the recommended duration of DAPT following DP-DES implantation is 12 months, with lifelong continuation of aspirin.[58] Short-term DAPT (6 months) has been proposed for BP-DES implantation due to improved arterial healing in the stented segment. The NIPPON trial found that 6-month and 18-month DAPT conferred equivocal safety and efficacy profiles in patients receiving BP-DES, with comparable rates of ST (0.1% versus 0.1%; p=1.00), cardiac death (0.2% versus 0.5%; p=0.39), and all-cause death (0.4% versus 1.0%; p=0.09).[59] Patients with poor compliance or high bleeding risk might theoretically benefit from BP-DES due to the shortened duration of DAPT.

Figure 1: Features of Orsiro biodegradable polymer drug-eluting stents



BIOlute = bioabsorbable poly-L-lactide eluting a limus drug; CoCr = cobalt chromium; proBIO = amorphous silicon carbide.

Ultrathin Orsiro biodegradable polymer drug-eluting stents

Ultrathin Orsiro BP-DES are based on a cobalt-chromium stent platform in a double-helix structure, with helical meanders, longitudinal connectors, and wedge-shaped transitions.[60] The metal alloy cobalt-chromium allows for thinner struts, which provide greater flexibility for effective stent delivery.[61] During stent expansion, the double-helix structure adapts to the vessel curvature without unnatural straightening.[62] This design feature also provides high radial strength to prevent longitudinal compression and foreshortening throughout the entire length of the stent.[63]

Orsiro BP-DES have a hybrid coating consisting of active and passive components to improve biocompatibility (*Figure 1*). The outer layer contains a BIOlute active coating (Biotronik, Bülach, Switzerland) that is made from biodegradable poly-L-lactic acid (PLLA) loaded with sirolimus.[64] The PLLA undergoes metabolism via the Krebs cycle into carbon dioxide and water, and completely degrades over 12–15 months.[65] The slow degradation of PLLA allows for the controlled release of sirolimus, since the drug elution period is shorter than the polymer degradation period. The release of sirolimus occurs at a dose of 1.4 µg/mm^2 over 3 months.[66] A histopathology study showed that PLLA SES had a significantly reduced neointimal area at 180 days compared with durable polymer SES (1.8 ± 1.2 versus 3.0 ± 1.5 mm^2; p=0.01). The investigators also reported that PLLA SES had sufficient sirolimus vascular tissue concentration, reduced inflammation, and improved re-endothelialisation compared with durable polymer SES. Furthermore, the BIOlute active coating has an abluminal thickness of 7.5 µm and a luminal thickness of 3.5 µm.[67] This asymmetric circumferential distribution ensures adherence of the polymer coating to the stent platform in

Table 2: Findings of clinical studies related to Orsiro biodegradable polymer drug-eluting stents

Study name	Year	Study type	Follow-up (months)	Stent comparator type	Patients (n)		Outcomes	Conclusion
					Orsiro BP-DES	Stent comparator		
BIOFLOW I[75]	2013	First-in-man study	12	N/A	30	N/A	– ST: 0% – MI: 0% – Cardiac death: 3.3% – TLR: 6.7%	N/A
BIOFLOW II[76]	2015	Non-inferiority RCT	12	Xience EES	298	154	– Definite or probable ST: 0% versus 0% – MI: 3.1% versus 2.6%; p=0.80 – Cardiac death: 0.7% versus 0.7%; p=0.98 – All-cause death: 1.0% versus 0.7%; p=0.71 – TLR: 3.8% versus 5.4%; p=0.46 – In-stent LLL at 9 months: 0.10 ± 0.32 mm versus 0.11 ± 0.29 mm; p=0.98	Non-inferior
BIOFLOW III[77]	2016	All-comers registry analysis	12	N/A	1,356	N/A	– Definite ST: 0.2% – MI: 2.7% – Cardiac death: 1.3% – TLR: 3.0%	N/A
SORT OUT VII[56]	2016	Non-inferiority RCT	12	Nobori BP-DES	1,261	1,264	– Definite ST: 0.4% versus 1.2%; p=0.03 – MI: 1.6% versus 2.4%; p=0.16 – Cardiac death: 1.3% versus 1.4% p=0.75 – All-cause death: 3.0% versus 2.2%; p=0.21 – TLR: 2.0% versus 2.9%; p=0.13	Non-inferior Definite ST lower with Orsiro BP-DES than Nobori BP-DES
ORIENT[78]	2017	Non-inferiority RCT	12	Resolute Integrity ZES	250	122	– Definite or probable ST: 0% versus 0% – MI: 0% versus 0.8%; p=0.13 – Cardiac death: 1.2% versus 0.8%; p=0.74 – All-cause death: 1.6% versus 0.8%; p=0.53 – TLR: 1.2% versus 2.5%; p=0.37 – In-stent LLL at 9 months: 0.06 mm (–0.09–0.24) versus 0.12 mm (–0.07–0.32); p=0.21	Non-inferior
PRISON IV[79]	2017	Non-inferiority RCT (chronic total occlusion)	12	Xience EES	165	165	– Definite or probable ST: 0.6% versus 0.6% – MI: 0.6% versus 0.6% – Cardiac death: 0.6% versus 1.2% – All-cause death: 0.6% versus 1.8% – TLR: 10.5% versus 4.0%; p=0.04 – In-stent LLL at 9 months: 0.12 ± 0.59 mm versus 0.07 ± 0.46 mm; p=0.52	Non-inferior TLR higher with Orsiro BP-DES than Xience EES
BIOSCIENCE[80]	2018	Non-inferiority RCT	60	Xience EES	1,063	1,056	– Definite or probable ST: 6.3% versus 7.7%; p=0.26 – MI: 10.4% versus 12.3%; p=0.23 – Cardiac death: 8.6% versus 7.5%; p=0.57 – All-cause death 14.1% versus 10.3%; p=0.02 – TLR: 11.5% versus 10.9%; p=0.61	Non-inferior All-cause death higher with Orsiro BP-DES than Xience EES
BIO-RESORT[81]	2018	Non-inferiority RCT	24	Resolute Integrity ZES	1,169	1,173	– Definite or probable ST: 0.6% versus 0.8%; p=0.62 – MI: 3.1% versus 3.6%; p=0.50 – Cardiac death: 1.3% versus 1.5%; p=0.73 – All-cause death: 2.6% versus 3.3%; p=0.33 – TLR: 2.2% versus 3.0%; p=0.24 – TLR beyond 12 months: 0.6% versus 1.5%; p=0.04	Non-inferior TLR beyond 12 months lower with Orsiro BP-DES than Resolute Integity ZES
BIONYX[82]	2018	Non-inferiority RCT	12	Resolute Onyx ZES	1,245	1,243	– Definite or probable ST: 0.7% versus 0.1%; p=0.01 – MI: 1.6% versus 1.6%; p=0.97 – Cardiac death: 1.1% versus 0.6%; p=0.18 – All-cause death: 2.1% versus 1.6%; p=0.37 – TLR: 2.0% versus 2.5%; p=0.35	Non-inferior Definite or probable ST higher with Orsiro BP-DES than Resolute Onyx ZES

Table 2: Cont.

Study name	Year	Study type	Follow-up (months)	Stent comparator type	Patients (n)		Outcomes	Conclusion
					Orsiro BP-DES	Stent comparator		
BIOFLOW V[83]	2018	Non-inferiority RCT	24	Xience EES	884	450	– Definite very late ST: 0.1% versus 1.0%; p=0.045 – MI: 5.3% versus 9.5%; p=0.01 – Cardiac death: 0.6% versus 0.5%; p=1.00 – All-cause death: 1.9% versus 2.2%; p=0.83 – TLR: 2.6% versus 4.9%; p=0.04 – TLF: 7.5% versus 11.9%; p=0.02	Non-inferior Definite very late ST, MI, TLR, and TLF lower with Orsiro BP-DES than Xience EES
BIOSTEMI[84]	2019	Superiority RCT	12	Xience EES	649	651	– Definite or probable ST: RR, 0.69; 95% CrI, 0.32–1.69 – MI: RR, 1.21; 95% CrI, 0.60–2.46 – Cardiac death: RR, 0.77; 95% CrI, 0.43–1.40 – All-cause death: RR, 0.97; 95% CrI, 0.58–1.62 – TLR: RR, 0.57; 95% CrI, 0.28–1.12 – TLF: RR, 0.59; 95% CrI, 0.37–0.94	Non-superior TLF lower with Orsiro BP-DES than Xience EES

Values are mean ± standard deviation or median (interquartile range).
BP-DES = biodegradable polymer drug-eluting stents; CrI = credibility interval; EES = everolimus-eluting stents; LLL = late lumen loss; MI = myocardial infarction; N/A = not available; RCT = randomised controlled trial; RR = risk ratio; ST = stent thrombosis; TLF = target lesion failure; TLR = target lesion revascularisation; ZES = zotarolimus-eluting stents.

Table 3: Findings of landmark trials related to other types of biodegradable polymer drug-eluting stents

Trial name	Year	Follow-up (months)	Stent type		Patients (n)		Outcomes	Conclusion
			BP-DES	DP-DES	BP-DES	DP-DES		
Separham et al.[85]	2011	12	BioMatrix BES	Xience EES	100	100	– ST: 0% versus 0% – MI: 0% versus 0% – Cardiac death: 0% versus 0%	Non-inferior
Xu et al.[86]	2011	24	Tivoli SES	Endeavor ZES	168	156	– Definite or probable ST: 0.6% versus 0%; p=1.00 – MI: 2.4% versus 1.3%; p=0.69 – Cardiac death: 0.6% versus 0%; p=1.00 – All-cause death: 0.6% versus 0%; p=1.00 – TLR: 4.2% versus 9.6%; p=0.0495	Non-inferior TLR lower with Tivoli SES than Endeavour ZES
EVOLVE FHU[87]	2013	24	Synergy EES	Promus Element EES	193	98	– Definite or probable ST: 0% versus 0% – MI: 3.1% versus 0% – Cardiac death: 1.0% versus 0% – All-cause death: 3.6% versus 0%	Non-inferior
TARGET I[88]	2013	12	Firehawk SES	Xience EES	227	231	– Definite or probable ST: 0% versus 0% – MI: 1.3% versus 2.2%; p=0.72 – Cardiac death: 0.4% versus 0% – All-cause death: 0.4% versus 0.9%; p=1.00 – TLR: 0.4% versus 0.4%; p=1.00	Non-inferior
CENTURY II[89]	2014	9	Ultimaster SES	Xience EES	551	550	– ST: 0.9% versus 0.9%; p=0.99 – MI: 2.0% versus 2.7%; p=0.43 – Cardiac death: 0.9% versus 1.1%; p= 0.76 – All-cause death: 1.3% versus 1.6%; p=0.61 – TLR: 2.7% versus 2.2%; p=0.56	Non-inferior
LONG-DES V[90]	2014	12	Nobori BES	Promus Element EES	245	255	– Definite or probable ST: 1.2% versus 0%; p=0.12 – MI: 13.9% versus 15.7%; p=0.53 – Cardiac death: 0.8% versus 0.4%; p=0.62 – All-cause death: 0.8% versus 0.4%; p=0.62 – TLR: 3.3% versus 2.0%; p=0.44	Non-inferior
BASKET-PROVE II[91]	2015	24	Nobori BES	Xience EES	765	765	– Definite or probable ST: 0.4% versus 0.7%; p=0.48 – MI: 2.4% versus 2.7%; p=0.64 – Cardiac death: 1.3% versus 0.9%; p=0.46 – All-cause death: 2.6% versus 2.2%; p=0.61	Non-inferior

Table 3: Cont.

Trial name	Year	Follow-up (months)	Stent type		Patients (n)		Outcomes	Conclusion
			BP-DES	DP-DES	BP-DES	DP-DES		
DESSOLVE II[92]	2015	9	MiStent SES	Endeavor ZES	123	61	– ST: 0.9% versus 1.7% – MI: 2.6% versus 3.3% – Cardiac death: 0.9% versus 1.7% – All-cause death: 0.9% versus 1.7% – TLR: 0.9% versus 1.7%	Non-inferior
EVERBIO II[93]	2015	9	BioMatrix BES	Promus Element EES	80	80	– Definite or probable ST: 0% versus 0% – MI: 0% versus 1.3% – Cardiac death: 0% versus 0% – All-cause death: 0% versus 3.8% – TLR: 5.0% versus 13.8%	Non-inferior
EVOLVE II[94]	2015	12	Synergy EES	Promus Element EES	846	838	– Definite or probable ST: 0.4% versus 0.6%; p=0.50 – MI: 5.4% versus 5.0%; p=0.68 – Cardiac death: 0.5% versus 0.9%; p=0.34 – All-cause death: 1.1% versus 1.1%; p=0.95 – TLR: 2.6% versus 1.7%; p=0.21	Non-inferior
SORT OUT VI[97]	2015	36	BioMatrix BES	Resolute Integrity ZES	1,497	1,502	– Definite or probable ST: 1.2% versus 1.3%; p=0.86 – MI: 4.7% versus 4.1%; p=0.49 – Cardiac death: 3.4% versus 2.7%; p=0.31 – All-cause death: 7.6% versus 7.6%; p=0.96 – TLR: 5.5% versus 5.4%; p=0.90	Non-inferior
ISAR-TEST 4[95]	2016	60	Yukon Choice PC SES	Xience EES	1,299	652	– Definite or probable ST: 1.2% versus 1.4%; p=0.67 – MI: 5.5% versus 5.0%; p=0.67 – Cardiac death: 5.2% versus 5.2%; p=0.89 – All-cause death: 14.7% versus 14.8%; p=0.95 – TLR: 13.9% versus 12.6%; p=0.46	Non-inferior
COMPARE II[96]	2017	60	Nobori BES	Xience EES	1,795	912	– Definite or probable ST: 1.7% versus 1.6%; p=0.96 – MI: 7.6% versus 7.0%; p=0.56 – Cardiac death: 4.6% versus 3.9%; p=0.45 – All-cause death: 8.6% versus 8.2%; p=0.72 – TLR: 7.9% versus 7.1%; p=0.47	Non-inferior
DESSOLVE III[98]	2018	12	MiStent SES	Xience EES	703	695	– Definite or probable ST: 0.7% versus 0.9%; p=0.76 – MI: 2.4% versus 2.2%; p=0.73 – Cardiac death: 2.0% versus 1.6%; p=0.55 – All-cause death: 3.6% versus 2.6%; p=0.29 – TLR: 3.4% versus 4.1%; p=0.48	Non-inferior
NEXT[99]	2018	60	Nobori BES	Xience EES	1,283	1,285	– Definite or probable ST: 0.5% versus 0.3%; p=0.52 – MI: 5.2% versus 4.8%; p=0.72 – Cardiac death: 4.4% versus 3.9%; p=0.54 – All-cause death: 11.7% versus 12.6%; p=0.51 – TLR: 9.8% versus 9.3%; p=0.79	Non-inferior
TARGET All Comers[100]	2018	12	Firehawk SES	Xience EES	823	830	– Definite or probable ST: 1.3% versus 1.3%; p=0.99 – MI: 5.4% versus 4.8%; p=0.62 – Cardiac death: 1.2% versus 0.9%; p=0.60 – All-cause death: 2.2% versus 2.2%; p=0.98 – TLR: 2.0% versus 3.0%; p=0.20	Non-inferior
TALENT[101]	2019	12	Supraflex SES	Xience EES	720	715	– Definite or probable ST: 0.8% versus 0.9%; p=1.00 – MI: 3.1% versus 3.7%; p=0.55 – Cardiac death: 1.0% versus 0.3%; p=0.10 – All-cause death: 2.0% versus 0.6%; p=0.02 – TLR: 3.5% versus 4.3%; p=0.50	Non-inferior All-cause death higher with Supraflex SES than Xience EES

BES = biolimus-eluting stents; BP-DES = biodegradable polymer drug-eluting stents; DP-DES = durable polymer drug-eluting stents; EES = everolimus-eluting stents; MI = myocardial infarction; SES = sirolimus-eluting stents; ST = stent thrombosis; TLR = target lesion revascularisation; ZES = zotarolimus-eluting stents.

regions of increased stress during stent expansion, while providing higher drug capacity on the abluminal side than the luminal side.[68] The inner layer contains a proBIO passive coating (Biotronik, Bülach, Switzerland) that eliminates the interaction between the metal alloy and surrounding tissue by covering the entire stent surface.[69] The proBIO passive coating is made from a thin layer (80 nm) of silicon carbide.[70] The silicon carbide has semi-conductor properties that provide a diffusion barrier between the metal ions and cellular proteins to reduce thrombogenicity and promote re-endothelialisation.[71]

Pre-clinical studies

The unique features of Orsiro BP-DES have been investigated in animal studies. An *in vivo* study involving a porcine model of coronary stent implantation showed that biodegradable polymer SES had significantly reduced neointimal area (1.8 ± 2.2 versus 3.0 ± 1.5 mm^2; p=0.01) and area stenosis (26.4 ± 15.2% versus 40.1 ± 19.5%; p=0.04) at 180 days compared with durable polymer SES.[72] An *ex vivo* study involving a porcine carotid to jugular arteriovenous shunt model found that Orsiro BP-DES and Xience EES (the latter manufacturerd by Abbott Vascular, Santa Clara, CA, USA) conferred equivocal thrombogenicity profiles, with comparable fluorescence positive area (mean difference, 2.95; 95% confidence interval [CI], –1.26 to 7.15; p=0.286).[73] The fluorescence positive area examined under confocal microscopy corresponds to the extent of platelet aggregation.[74]

Clinical studies

The safety and efficacy profiles of Orsiro BP-DES have been evaluated in various studies. *Table 2* summarises the findings of clinical studies related to Orsiro BP-DES.[56,75–84] Overall, the randomised trials showed that Orsiro BP-DES were non-inferior to second-generation DP-DES, including Xience EES and Resolute Integrity™ ZES (the latter manufacturerd by Medtronic, Santa Rosa, CA, USA). The FDA approved the use of Orsiro BP-DES in patients with CAD based on promising results in recent trials, such as BIOFLOW V[83] and BIOSTEMI.[84] Both of these trials found that Orsiro BP-DES had a significantly reduced risk of target lesion failure, which is a composite of MI, cardiac death, and TLR, compared with Xience EES. *Table 3* summarises the findings of landmark trials related to other types of BP-DES.[85–101] Overall, the randomised trials showed that other types of BP-DES were also non-inferior to second-generation DP-DES. These devices included Nobori BP-DES and Synergy™ BP-DES (the latter manufacturerd by Boston Scientific, Marlborough, MA, USA).

A recent meta-analysis of 11,176 patients found that Orsiro BP-DES and second-generation DP-DES conferred equivocal safety and efficacy profiles, with comparable rates of definite or probable ST (odds ratio [OR], 0.77; 95% CI, 0.53–1.12; p=0.18), MI (OR, 0.79; 95% CI, 0.63–1.00; p=0.05), all-cause death (OR, 1.17; 95% CI, 0.84–1.64), and target lesion failure (OR, 0.87; 95% CI, 0.72–1.05; p=0.16).[102] These findings offered reassurance about the clinical performance of Orsiro BP-DES. However, this meta-analysis did not include the recent BIOSTEMI trial, which would have provided the latest clinical evidence to date.[84]

Conclusion

Ultrathin Orsiro BP-DES showcase the latest innovations in coronary stent technology. The thin-strut cobalt-chromium stent platform with a biodegradable polymer coating enhances biocompatibility by eliminating the potential stimulus for a chronic inflammatory response in the vessel wall. The latest clinical evidence at the time of writing demonstrated that Orsiro BP-DES conferred comparable safety and efficacy profiles to the current gold standard second-generation DP-DES. In light of the recent FDA approval, Orsiro BP-DES represents a suitable alternative to the second-generation DP-DES in patients with CAD. Further randomised trials with greater length of follow-up and larger patient populations are warranted to establish the purported benefits of Orsiro BP-DES. ❑

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