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Ultrathin StrutBioresorbable polymer stent sets new standard in drug-eluting stent technology

BIOFLOW V trial: Three-year results

Interventional cardiologists have, for the last few years, assumed that DES technology, with the contemporary drug eluting stents has reached a plateau, with very low levels of events. It is therefore a pleasant surprise for us to see the results of the **Bioflow V** trial, where, the Orsiro stent, an Ultrathin strut DES (60um), with a Biodegradable polymer, has shown an improvement on the already impressive data from the contemporary thin strut (81um) Xience stent.

The **Bioflow V** trial is a tremendous achievement for the Orsiro stent, as it is a clinical trial that includes all types of patients routinely seen in daily clinical practice, including complex patients, bifurcation lesions, diabetics and other high risk patients. The data is robust up to 3 years and even more impressive is that the results for the Orsiro stent are better than a stent which until now was considered the best available.

The superiority of the Ultra-thin strut Orsiro stent is further strengthened by the recent data presented at the ACC meeting, showing that Orsiro outperforms all of the 3 contemporary durable polymer DES, namely: Xience, Resolute Integrity and Resolute Onyx.

It is intriguing to postulate whether the impressive performance of the Orsiro stent is due to the unique bioresorbable polymer or due to the ultra-thin struts or due to some other factor with this particular stent, as it has also shown superior benefit in STEMI patients in another trial (BIOSTEMI trial).

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LEARNING OBJECTIVES

You will learn:

- How innovation in stent technology is improving outcomes in elective and urgent PCI
- Which patients with complex angiography do best with ultrathin bioresorbable polymer stents (BP-SES)
- The latest from the 2020 ACC on BP-SES versus durable polymer stents (DP-DES)
- The latest 3-year results from BIOFLOW V with further reductions in target vessel MI, target lesion failure and stent thrombosis.

The ultrathin bioresorbable polymer drug-eluting stent (DES) with sirolimus is setting a new standard in DES technology, following the publication of the three-year results of the BIOFLOW V trial.[1] This is an important development, as long-term clinical safety and efficacy are key to progress and improvement in patient outcomes.

The BIOFLOW V trial* was an international, randomised, controlled study comparing clinical outcomes among patients undergoing percutaneous coronary intervention with an ultrathin-strut (60µm) bioresorbable polymer sirolimus-eluting stent (BP-SES) (Orsiro, Biotronik, Bülach, Switzerland) to those of patients who received a contemporary thin-strut (81µm) durable polymer everolimus-eluting stent (DP-EES) (Xience, Abbott Vascular, Santa Clara, California) (Figure 1).

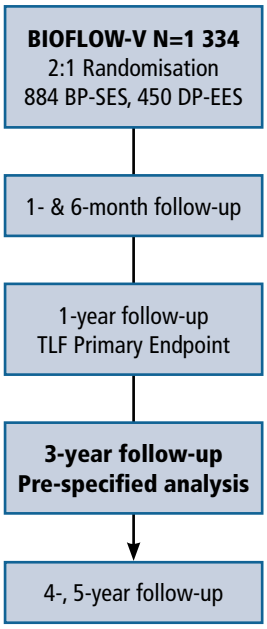
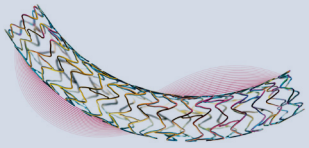


Figure 1. BIOFLOW V trial design

*Biotronik prospective randomised multicentre study to assess the safety and effectiveness of the Orsiro sirolimus-eluting coronary stent system in the treatment of patients with up to three de novo or restenotic coronary artery lesions.



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BIOTRONIK

Patients included in the study were undergoing elective and urgent percutaneous coronary interventions for ≤3 *de novo* native coronary artery lesions in a maximum of two native target vessels. Non-STEMI, haemodynamically stable myocardial infarction (MI) and acute coronary syndrome patients were eligible for enrolment.[2] Patient characteristics at baseline are shown in Table 1.

Table 1. Patients in BIOFLOW V

	BP-SES (n=884, 1 051 lesions)	DP-EES (n=450, 561 lesions)
Age, years	64.5 ± 10.3	64.6 ± 10.7
Female	25.3 (224/884)	27.1 (122/450)
Hypertension	79.7 (696/873)	80.5 (354/440)
Hyperlipidaemia	78.9 (695/881)	82.4 (370/449)
Diabetes mellitus	34.0 (300/883)	37.0 (166/449)
Insulin-requiring	10.4 (92/883)	11.1 (50/449)
Prior myocardial infarction	27.4 (238/869)	25.9 (115/444)
Prior stroke or TIA	5.5 (49/884)	4.5 (20/448)
Renal disease	7.9 (70/883)	7.6 (34/450)
Prior coronary revascularisation	41.0 (360/877)	37.1 (165/445)
Prior PCI	36.8 (323/877)	33.0 (147/445)
Prior CABG	7.1 (62/877)	5.2 (23/445)
Current tobacco use	23.6 (209/884)	22.7 (102/450)
Clinical presentation		
Documented silent ischaemia	12.3 (109/884)	13.6 (61/449)
Stable angina	48.4 (428/884)	47.4 (213/449)
Unstable angina	39.3 (347/884)	39.0 (175/449)
Acute coronary syndrome*	51.4 (454/884)	49.6 (223/450)
Target lesion vessel, no./total no. of target lesions		
Left anterior descending	41.0 (431/1 051)	41.2 (231/561)
Left circumflex	26.5 (279/1 051)	26.0 (146/561)
Right	32.4 (341/1 051)	32.8 (184/561)
Angiographic complexity		
Reference vessel diameter, mm	2.59 ± 0.54	2.60 ± 0.58
Lesion length, mm	13.3 ± 7.6	13.2 ± 7.7
Bifurcation lesion	14.8 (156/1 051)	15.0 (84/561)
Thrombus	1.0 (11/1 051)	0.9 (5/561)
Calcification, moderate/severe	24.0 (252/1 051)	26.7 (150/561)
Vessel tortuosity, moderate/severe	58.8 (618/1 051)	61.5 (345/561)
ACC/AHA lesion class B2/C	72.6 (763/1 051)	75.9 (426/561)
Number of target lesions/patient†	1/2 ± 0.4	1.3 ± 0.5
Number of stents/patient†	1.3 ± 0.7	1.5 ± 0.9
Total study stent length, mm†‡	26.8 ± 14.7	29.5 ± 17.5
Patients with overlapping stents	9.4 (83/884)	15.0 (67/448)
Stent length/lesion	20.8 ± 9.1	21.8 ± 10.5

Values are mean ±SD or % (n/N). The data shown are for patients who were randomised to receive a study stent.
*Acute coronary syndrome is defined as subjects with unstable angina or any elevated cardiac enzymes at baseline (any pre-procedure creatine kinase [CK], CK-MB, or troponin out of normal range).
†Statistically significant differences between groups. Target-lesion characteristics as assessed by an independent angiographic core laboratory.
‡The length of the individual study stents summed per patient.
ACC/AHA = American College of Cardiology/American Heart Association; BP-SES = bioresorbable polymer sirolimus-eluting stent; CABG = coronary artery bypass grafting; DP-EES = durable polymer everolimus-eluting stent; PCI = percutaneous coronary intervention; TIA = transient ischaemic attack.

Results

The three-year results show that Orsiro outperformed Xience, a contemporary second-generation DP-EES over the long term (Figure 2).

"The out-performance of this ultrathin BP-SES, in a complex patient population undergoing percutaneous coronary intervention, suggests a new direction in improving next-generation DES technology."

Dr David Kandzari (Atlanta, USA)

BIOFLOW V: Two- and three-year outcomes		
Stent model	**BP-SES (N=88)**	**DP-EES (N=450)**
Stent material*†	L-605 Cobalt-Chromium	L-605 Cobalt-Chromium
Polymer type‡	Bioresorbable polymer, poly-L-lactic acid (PLLA)	Durable polymer, A non-erodible copolymer, poly (vinylidene fluoride-cohexafluoropropylene) (PVDF-HFP)
Strut thickness‡	60µm§	81µm
Antiproliferative drug‡	Sirolimus (1.4µg/mm^2), >80% eluted in first 90 days	Everolimus (100µg/cm^2), 100% drug release within 4 months

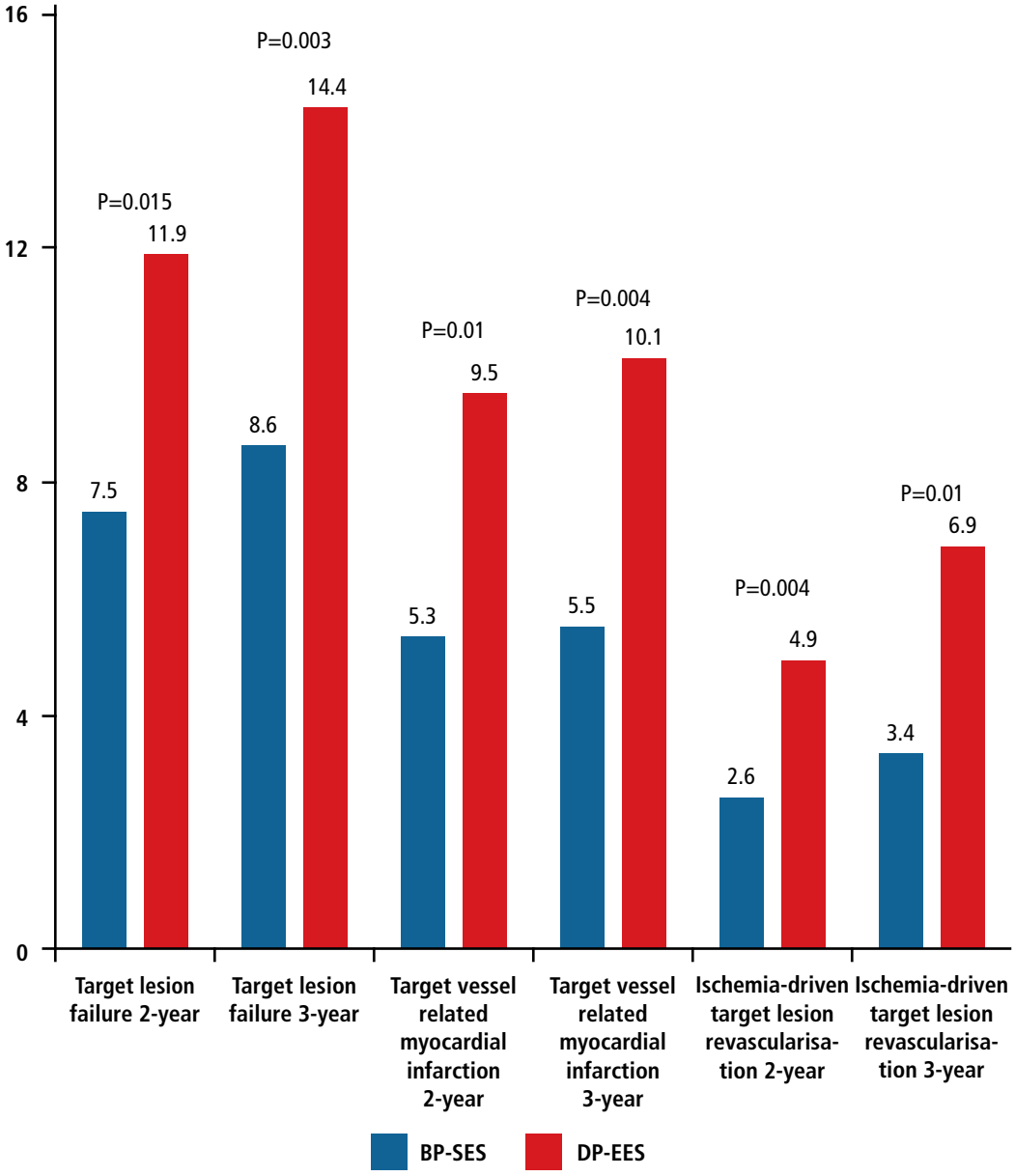

Figure 2. Central illustration – Comparison of an ultrathin-strut BP-SES and a thin-strut DP-EES: summary of two-year and three-year outcomes

*BP-SES Instructions for Use. †DP-EES Instructions for Use. ‡Kandzari *et al.* (8). §For 2.25mm to 3.0mm diameter stents, thin struts for >3.0mm diameter stents. Target lesion failure includes cardiac death, target vessel-related MI, or ischaemia-driven target lesion revascularisation. Major adverse cardiac events include all-cause death, MI (Q-wave or non–Q-wave), and any ischaemia-driven target lesion revascularisation. Target vessel failure includes cardiac death, target vessel MI or ischaemia-driven target vessel revascularisation. BP-SES ¼ bioresorbable polymer sirolimus-eluting stent; DP-EES 1/4 durable polymer everolimus-eluting stent.

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Evaluation of results

In this landmark analysis over three years, significant differences in target vessel MI, target lesion failure (TLF) and definite late/very late stent thrombosis were observed, favouring treatment with a BP-SES.

Table 2. BIOFLOW V – stent thrombosis over three years

Stent thrombosis events	BP-SES (N=884)	DP-EES (N=450)	P-value
Definite	0.5%	1.5%	0.094
Probable	0	0	–
Any ARC (Definite/probable/possible)	1.0%	2.0%	0.185
Definite/probable stent thrombosis			
Early	0.3%	0.2%	1.00
Late (>30 days and ≤1 year)	0.1%	0.5%	0.26
Very late (>1 year and ≤3 years)	0	0.7%	0.038
Late/very late (>30 days and ≤3 years)	0.1%	1.2%	0.018

ARC = Academic Research Consortium
DAPT = Dual antiplatelet therapy

Cardiac death or MI rates were 8.16% versus 12.4% for the BP-SES and DP-EES, respectively. Over the past decade, endpoint event rates have migrated lower due to improvements in metal alloys, changes in stent architecture and bioresorbable polymers. Dr David Kandzari (Atlanta, USA), principal investigator, pointed out that it had been widely believed that the safety and efficacy of DES had plateaued, but BIOFLOW V's results with the Orsiro cobalt-chromium metal stent, eluting sirolimus via a bioresorbable polymer coating, have now shown statistically significant lower event rates. "The out-performance of this ultrathin BP-SES, in a complex patient population undergoing percutaneous coronary intervention, suggests a new direction in improving next-generation DES technology," he said.

Summary of three-year BIOFLOW V data

- 40% lower TLF rate in favour of Orsiro
- 52% lower ischaemia-driven target lesion revascularisation rate
- 46% lower rate of target vessel myocardial infarction (TVMI)
- 90% lower late/very late definite/probable stent thrombosis

STOP PRESS: Further data from the American College of Cardiology (ACC) congress, March 2020

A meta-analysis of eight randomised clinical trials including more than 10 000 patients treated with either Orsiro BP-SES or DP-DES, presented at the 2020 ACC Congress[3] by Dr MR Monjur (Australia), showed that the BP-SES reduced TLF by 15%, compared to contemporary DP-DES such as Resolute Integrity, Xience and Resolute Onyx.

References

1. Kandzari DE, Koolen JJ, Doros G, *et al*. Ultrathin bioresorbable polymer sirolimus-eluting stents in patients undergoing coronary revascularisation: 3 year outcomes from the randomized BIOFLOW V Trial. *JACC Cardiovascular Interventions* 2020; **13**(4): Suppl 542.
2. Kandzari DE, Koolen JJ, Doros G, *et al*. Ultrathin bioresorbable polymer sirolimus-eluting stents versus thin durable polymer everolimus-eluting stents. *J Am Coll Cardiol* 2018: **72**: DOI: 10.1016/j.jacc.2018.09.019.
3. Monjur MR, Said CF, Bamford P, *et al*. Abstract 1253-039. Biodegradable polymer sirolimus-eluting stent (Orsiro) versus second generation durable polymer drug eluting stents: a meta-analysis of randomised trials. *J Am Coll Cardiol* 2020; **75**: Suppl 1. DOI: 10.1016/S0735-1097(20)31958-6.

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