Orsiro®

Comparison of Ultrathin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus-Eluting Durable Polymer Stents – BIOFLOW-V

Final outcomes of the pivotal FDA trial

Dr. David E. Kandzari, Piedmont Heart Institute, Atlanta, USA,
Dr. Jacques Koolen, Catharina Ziekenhuis, Eindhoven, Netherlands

BIOFLOW-V

Comparison of Ultrathin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus-Eluting Durable Polymer Stents – BIOFLOW-V

Design

Prospective, multicenter, 2:1 randomized controlled IDE (Investigational Device Exemption) trial.

Principal Investigators

Dr. David E. Kandzari, Piedmont Heart Institute, Atlanta, USA,

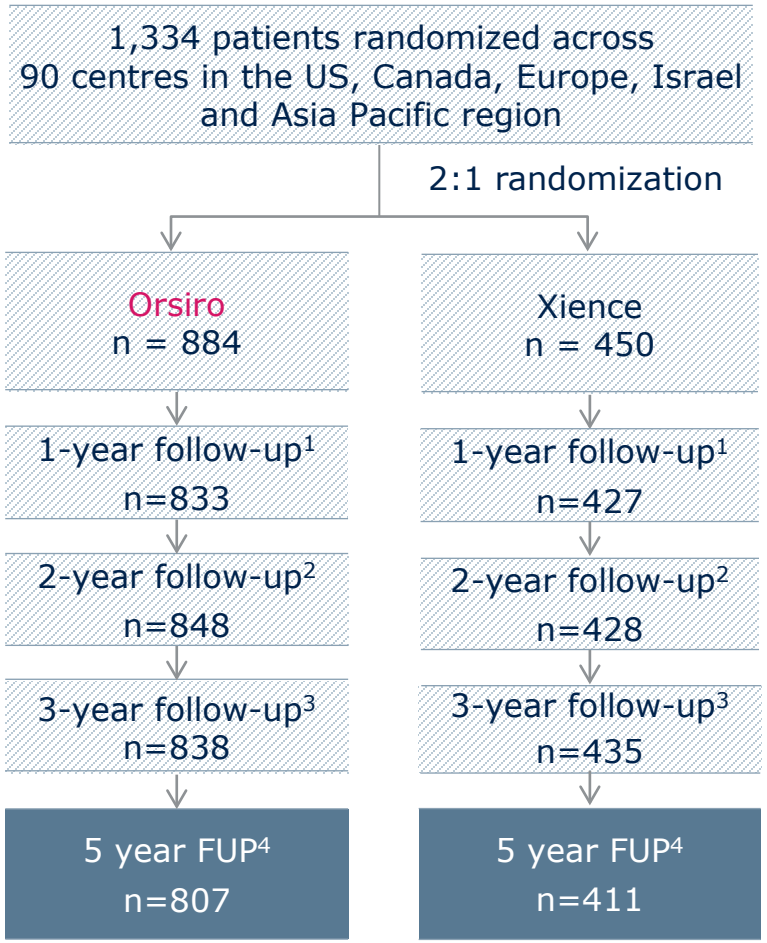
Dr. Jacques Koolen, Catharina Ziekenhuis, Eindhoven, Netherlands

Primary Endpoint

Target lesion failure, a composite of: cardiac death, target vessel myocardial infarction, or ischemia-driven target lesion revascularization, at 12 months.

Secondary Endpoint

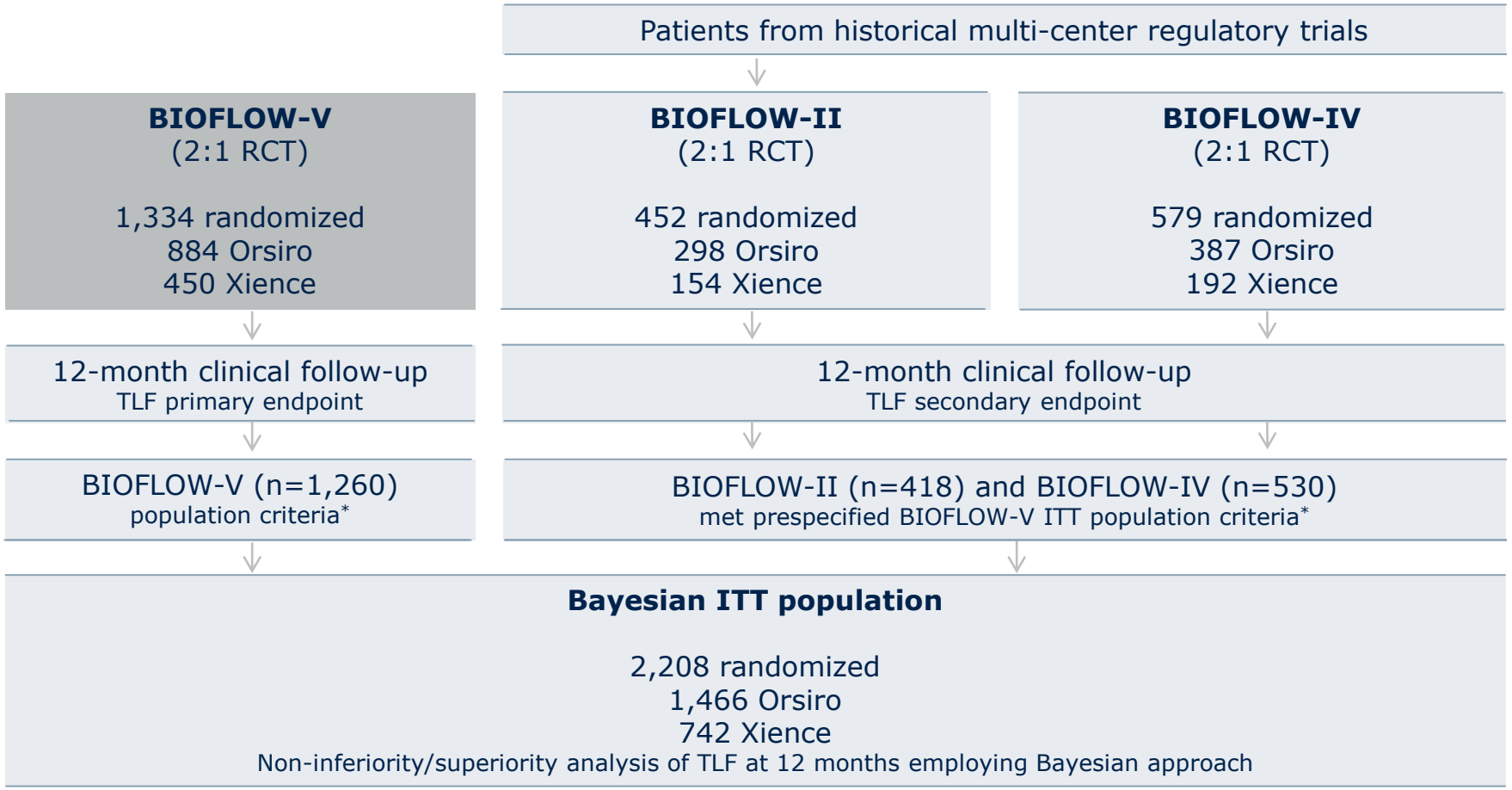
- Components of the primary endpoint
- MACE as a composite of all-cause death, MI or ischemia driven TLR
- Target Vessel Failure (TVF) and individual TVF components
- Stent thrombosis (all, definite, definite/ probable, probable, possible ST)



Sources: 1. Kandzari D et al. Lancet. 2017 Oct 21; 390(10105):1843-1852; 2. Kandzari D et al. Journal of American College of Cardiology (2018), doi: https//doi.org/10.1016/j.jacc.2018.09.019; 3. Kandzari D et al. J Am Coll Cardiol. Cardiovasc Interven. 2020, doi: 10.1016/j.jcin.2020.02.019. 4.Kandzari D et al. Submitted manuscript to JACC:2022 NCT02389946.

Bayesian Analysis

BIOFLOW-V



BIOFLOW-V ITT population criteria: BIOFLOW-V enrolment criteria, at least 330 days of follow-up or experienced an endpoint event prior to 330 days.

Source: Kandzari D 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, The Lancet, 2017

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Endpoints

BIOFLOW-V

Primary Endpoint

- Target Lesion Failure (TLF) at 12 months, defined as the composite of cardiovascular death, target vessel-related myocardial infraction (MI), or ischemia-driven TLR

Secondary Endpoints

- Major Adverse Cardiac Events (MACE) – composite of all-cause death, MI, or ischemia-driven TLR
- Target Vessel Failure Rate (TVF) – composite of all-cause death, target vessel-related MI, or ischemia driven TVR
- Individual components of composite endpoints at 30 days and 12 months
- Definite/probable stent thrombosis
- Device success – achievement of <30% diameter stenosis of the target lesion within the study stent
- Procedure success – final diameter stenosis <30% with the assigned stent and with no in-hospital MACE

Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017

Inclusion/Exclusion

BIOFLOW-V

Main Inclusion Criteria

- Age ≥ 18 years
- IHD, stable or unstable angina, or silent ischemia
- ≤ 3 de novo target lesions in ≤ 2 native target vessels (TV)
- RVD ≥ 2.25 mm and ≤ 4.0 mm
- LL ≤ 36 mm
- TIMI flow > 1
- Eligible for DAPT therapy (aspirin + P2Y12)
- Provided informed consent

Main Exclusion Criteria

- Recent (< 72 hours prior to procedure) STEMI or hemodynamically unstable NSTEMI/ ACS patients
- Chronic total occlusions, bypass grafts
- Bifurcations with side branch > 2.0 mm
- In-stent restenosis or active stent thrombosis
- LVEF < 30%
- Prior PCI within 30 days for (non-TV) or within 9 months (TV)
- Renal impairment > 2.5 mg/dL or 221 µmol/L or dialysis dependent
- Excessively tortuous/angulated or severely calcified (operator visual assessment)

Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017

Countries and Centers

BIOFLOW-V

- 13 Countries, 91 centers around the world
- Patients enrolled in North America (665), Europe (390), Israel (231), Asia (36), and Australia and New Zealand (12)
- Leading Enrollment Sites:

Institution	Country	Number enrolled
UZ Leuven-Campus Gasthuisberg	Belgium	57
Rambam Medical Center	Israel	55
Kaplan Medical Center(Clalith Health Services)	Israel	52
Rabin Medical Center	Israel	48
Universitares Herzzentrum Hamburg	Germany	44
Ein-Kerem Medical Center	Israel	43
Charleston Area Medical Health System	USA	39
Florida Hospital Pepin Heart Institute	USA	35
Cardiovascular Associates, Ltd.	USA	34
Columbia Presbyterian University Medical Center	USA	33
Sourasky Medical Center Tel Aviv	Israel	33
Thomas Hospital	USA	31
University Hospital Lausanne	Switzerland	31

Source: Kandzari D 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, The Lancet, 2017

Baseline Clinical Characteristics

BIOFLOW-V

	Orsiro (n = 884)	Xience (n = 450)
Age, years – mean ± SD	64.5 ± 10.3	64.6 ± 10.7
Female gender – n (%)	224 (25.3%)	122 (27.1%)
Hypertension – n (%)	696 (79.7%)	354 (80.5%)
Hyperlipidemia – n (%)	695 (78.9%)	370 (82.4%)
Diabetes mellitus – n (%)	300 (34.0%)	166 (37.0%)
Stroke or Transient Ischemic Attack – n (%)	49 (5.5%)	20 (4.5%)
Renal disease – n (%)	70 (7.9%)	34 (7.6%)
Prior PCI – n (%)	323 (36.8%)	147 (33.0%)
Prior CABG – n (%)	62 (7.1%)	23 (5.2%)
Current tobacco use – n (%)	209 (23.6%)	102 (22.7%)
Clinical presentation – n (%)		
Documented silent ischemia	109 (12.3%)	61 (13.6%)
Stable angina	428 (48.4%)	213 (47.4%)
Unstable angina	347 (39.3%)	175 (39.0%)
Acute coronary syndrome	454 (51.4%)	223 (49.6%)

Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017

Baseline Lesion Characteristics

BIOFLOW-V

	Orsiro (n = 1,051)	Xience (n = 561)
Target Lesion Vessel – n (%)		
Left anterior descending	431 (41.0%)	231 (41.2%)
Left circumflex	279 (26.6%)	146 (26.0%)
Right coronary artery	341 (32.5%)	184 (32.8%)
Reference vessel diameter, mm – mean ± SD	2.6 ± 0.5	2.6 ± 0.6
Bifurcation lesion – n (%)	156 (14.8%)	84 (15.0%)
Thrombus – n (%)	11 (1.1%)	5 (0.9%)
Moderate / severe calcification – n (%)	252 (24.0%)	150 (26.7%)
Moderate / severe tortuosity – n (%)	618 (58.8%)	345 (61.5%)
ACC-AHA Lesion Class B2/C – n (%)	763 (72.6%)	426 (75.9%)

Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017

Baseline Angiographic/Procedural Characteristics

BIOFLOW-V

	Orsiro (n=1,051)	Xience (n=561)
Lesion length, mm – mean ± SD	13.3 ± 7.6	13.2 ± 7.7
Reference vessel diameter, mm – mean ± SD	2.6 ± 0.5	2.6 ± 0.6
No. target lesions/pt*, mean ± SD	1.2 ± 0.4	1.3 ± 0.5
% diameter stenosis, pre, mean ± SD	55.4 ± 13.3	55.9 ± 13.5
% diameter stenosis, post, mean ± SD	7.1 ± 9.8	7.4 ± 9.8
Post-dilation performed	47.7%	46.2%
No. stents/lesion*, mean ± SD	1.07 ± 0.3	1.13 ± 0.4
Stent length/lesion, mean ± SD	20.8 ± 9.1	21.8 ± 10.5
Overlapping stents*	9.4%	15.0%

Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017

BIOFLOW-V - Published in The Lancet

BIOFLOW-V

Publication:

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Title:

Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a rondomised trial

Authors:

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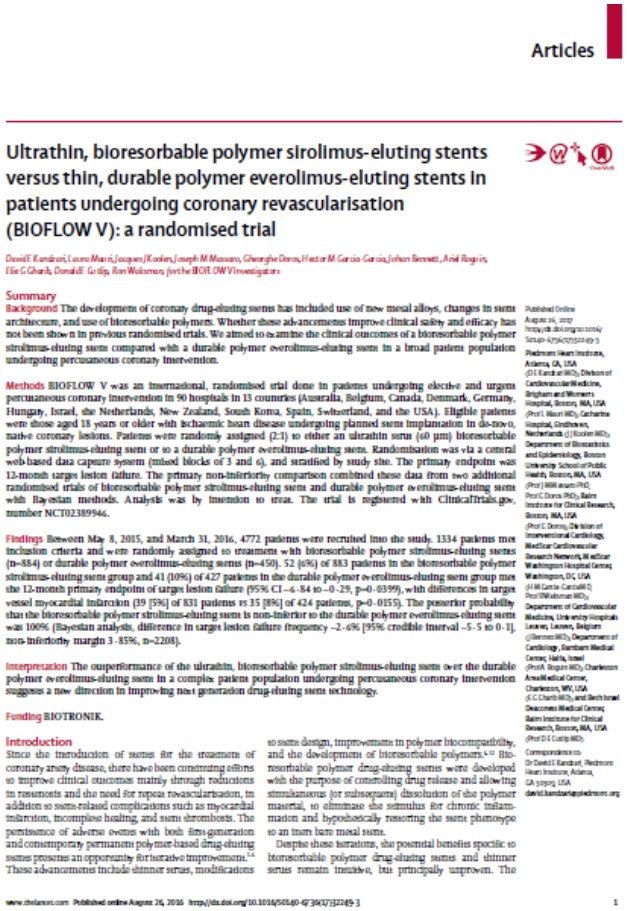
Conclusion:

In a large randomised trial, both TLF and target vessel-related MI were significantly lower among patients treated with BP SES versus DP EES. In Bayesian analysis, BP SES demonstrated unequivocal non-inferiority to DP EES at one year. The outperformance of this ultrathin BP SES in a complex patient population undergoing percutaneous coronary intervention suggest a new direction in improving the next generation DES technology.



Articles

Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a randomised trial

Summary

Background The development of coronary drug-eluting stents has included use of new metal alloys, changes in stent architecture, and use of bioresorbable polymers. Whether these advancements improve clinical safety and efficacy has not been shown in previous randomised trials. We aimed to examine the clinical outcomes of a bioresorbable polymer sirolimus-eluting stent compared with a durable polymer everolimus-eluting stent in a broad patient population undergoing percutaneous coronary intervention.

Methods BIOFLOW V was an international, randomised trial done in patients undergoing elective and urgent percutaneous coronary intervention in 90 hospitals in 13 countries (Australia, Belgium, Canada, Denmark, Germany, Hungary, Israel, the Netherlands, New Zealand, South Korea, Spain, Switzerland, and the USA). Eligible patients were those aged 18 years or older with ischaemic heart disease undergoing planned stent implantation in de-novo, native coronary lesions. Patients were randomly assigned (2:1) to either an ultrathin strut (60 μm) bioresorbable polymer sirolimus-eluting stent or to a durable polymer everolimus-eluting stent. Randomisation was via a central web-based data capture system (mixed blocks of 3 and 6), and stratified by study site. The primary endpoint was 12-month target lesion failure. The primary non-inferiority comparison combined these data from two additional randomised trials of bioresorbable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent with Bayesian methods. Analysis was by intention to treat. The trial is registered with ClinicalTrials.gov, number NCT02389946.

Findings Between May 8, 2015, and March 31, 2016, 4772 patients were recruited into the study. 1334 patients met inclusion criteria and were randomly assigned to treatment with bioresorbable polymer sirolimus-eluting stents (n=834) or durable polymer everolimus-eluting stents (n=450). 52 (6%) of 883 patients in the bioresorbable polymer sirolimus-eluting stent group and 41 (10%) of 427 patients in the durable polymer everolimus-eluting stent group met the 12-month primary endpoint of target lesion failure (95% CI −6·84 to −0·29, p=0·0399), with differences in target vessel myocardial infarction (39 [5%] of 831 patients vs 35 [8%] of 424 patients, p=0·0155). The posterior probability that the bioresorbable polymer sirolimus-eluting stent is non-inferior to the durable polymer everolimus-eluting stent was 100% (Bayesian analysis, difference in target lesion failure frequency −2·6% [95% credible interval −5·5 to 0·1], non-inferiority margin 3·85%, n=2208).

Interpretation The outperformance of the ultrathin, bioresorbable polymer sirolimus-eluting stent over the durable polymer everolimus-eluting stent in a complex patient population undergoing percutaneous coronary intervention suggests a new direction in improving next generation drug-eluting stent technology.

Funding BIOTRONIK.

Introduction

Since the introduction of stents for the treatment of coronary artery disease, there have been continuing efforts to improve clinical outcomes mainly through reductions in restenosis and the need for repeat revascularisation, in addition to stent-related complications such as myocardial infarction, incomplete healing, and stent thrombosis. The persistence of adverse events with both first-generation and contemporary permanent polymer-based drug-eluting stents presents an opportunity for iterative improvements.[1,2] These advancements include thinner struts, modifications to stent design, improvements in polymer biocompatibility, and the development of bioresorbable polymers.[3–10] Bioresorbable polymer drug-eluting stents were developed with the purpose of controlling drug release and allowing simultaneous (or subsequent) dissolution of the polymer material, to eliminate the stimulus for chronic inflammation and hypothetically restoring the stent phenotype to an inert bare metal stent.

Despite these iterations, the potential benefits specific to bioresorbable polymer drug-eluting stents and thinner struts remain inutile, but principally unproven. The

Source: Kandzari D et al , Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a rondomised trial, The Lancet, 2017

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Procedural Results

BIOFLOW-V

	Orsiro (n = 884)	Xience (n = 450)	P-Value
Lesion success*	1,102/1,107 (99.6%)	579/583 (99.3%)	0.505
Device success†	1,082/1,107 (97.7%)	566/583 (97.1%)	0.415
Procedure success‡	827/881 (93.9%)	401/445 (90.1%)	0.019

Procedural success was significantly higher with Orsiro, principally driven by a higher rate of in-hospital MI with Xience. Specifically, the peri-procedural MI was higher in the Xience group.

* Lesion success defined as attainment of < 30% residual stenosis of the target lesion using any percutaneous method.

† Device success defined as attainment of < 30% residual stenosis of the target lesion using the assigned study stent only.

‡ Procedure success defined as attainment of < 30% residual stenosis of the target lesion using the assigned study stent only without occurrence of in-hospital major adverse cardiac events (MACE; composite of all-cause death, Q-wave or non-Q-wave MI, and any clinical-driven TLR).

Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017

Results: 30-Day Outcomes

BIOFLOW-V

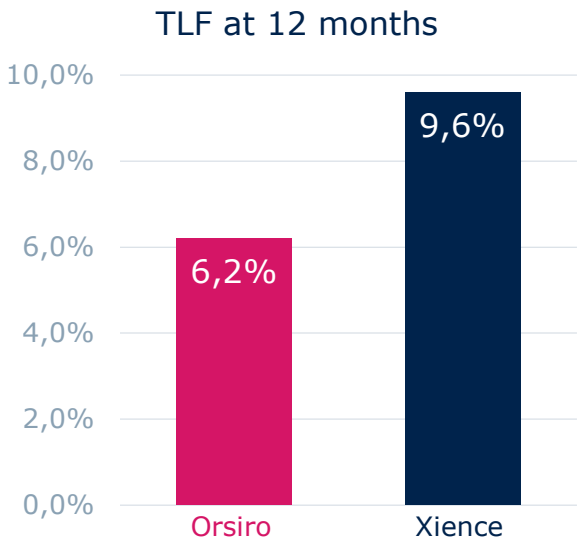
	Orsiro (n = 884)	Xience (n = 450)	P-Value
All-cause death	0.1%	0.2%	1.000
Myocardial Infarction	4.3%	6.9%	**0.050**
In-Hospital MI	3.9%	6.7%	**0.029**
TLR	0.5%	0.7%	0.694
Stent Thrombosis	0.3%	0.2%	1.000
TLF	4.2%	7.1%	**0.026**
TVF	4.3%	7.1%	**0.037**

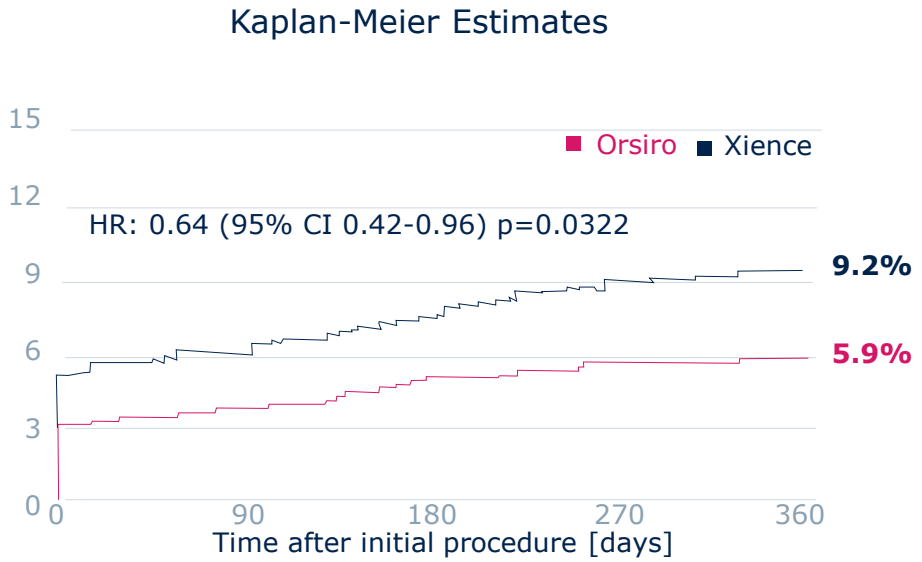
Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017

Results: 12-month Outcomes

BIOFLOW-V

	Orsiro (n = 884)	Xience (n = 450)	P-Value
Target lesion failure	52/833 (6.2%)	41/427 (9.6%)	**0.040**
Cardiac death	1/831 (0.1%)	3/425 (0.7%)	0.115
Target-vessel MI	39/831 (4.7%)	35/424 (8.3%)	**0.016**
Clinically-driven TLR	17/832 (2.0%)	10/422 (2.4%)	0.686





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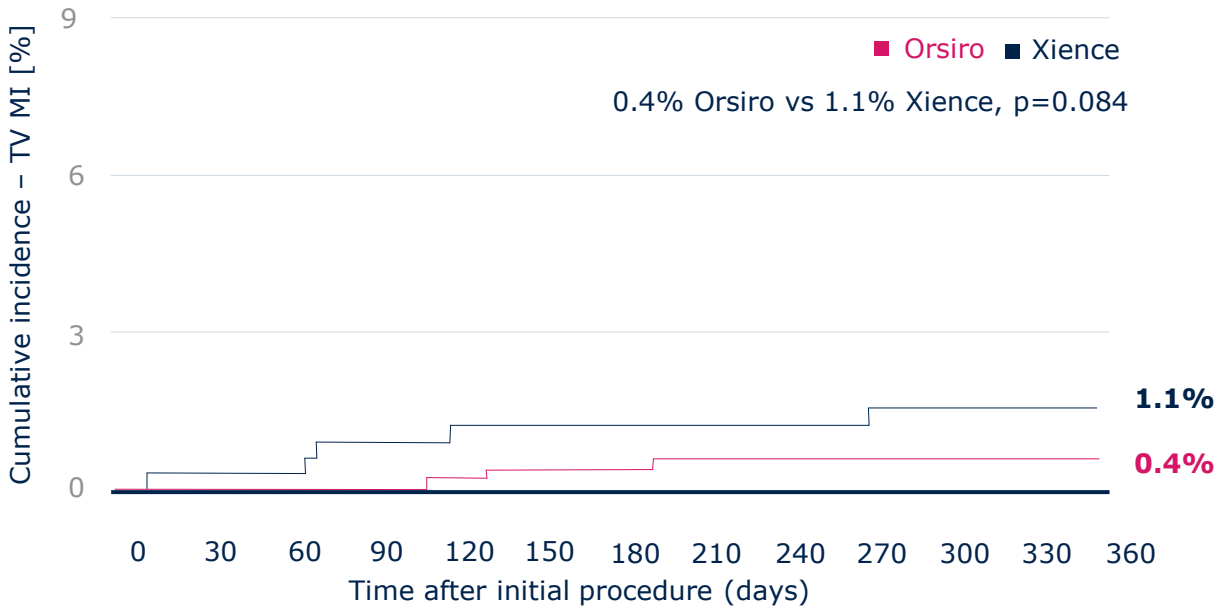
Results: 12-month Outcomes

BIOFLOW-V

Landmark Analysis TV-MI 30 days to 12 months



In a post-hoc landmark analysis of target vessel-related MI beyond 30 days of index revascularization, a numerically higher rate of target vessel-related MI among Xience treated patients persisted.

Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017

Results: 12-month Outcomes

BIOFLOW-V

	Orsiro (n = 884)	Xience (n = 450)	P-Value
Death from any cause	7/837 (0.8%)	6/428 (1.4%)	0.382
Any MI	41/832 (4.9%)	37/425 (8.7%)	**0.013**
Q-wave	1/831 (0.1%)	4/422 (1.0%)	**0.047**
Non-Q-wave	40/831 (4.8%)	34/425 (8.0%)	**0.031**
Cardiac death or any MI	42/833 (5.0%)	39/427 (9.1%)	**0.007**
MACE	59/839 (7.0%)	44/429 (10.3%)	0.051
Target-vessel failure	60/834 (7.2%)	45/427 (10.5%)	0.052
Target-vessel myocardial infarction	39/831 (4.7%)	35/424 (8.3%)	**0.016**
Clinically-driven target-vessel revascularization	27/833 (3·2%)	15/422 (3.6%)	0.7430

Source: Kandzari D et al, Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a rondomised trial, The Lancet, 2017

Results: 12-month Stent Thrombosis

BIOFLOW-V

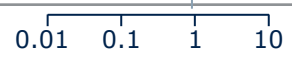
	Orsiro (n = 884)	Xience (n = 450)	P-Value
Timing of Event (Any ST)			
Acute (≤ 24 hours)	0.1%	0.0%	1.000
Sub-acute (> 24 hours and ≤ 30 days)	0.2%	0.2%	1.000
Late (> 30 days and ≤ 1 year)	0.1%	0.9%	**0.047**
Stent Thrombosis			
Any Stent Thrombosis	0.5%	1.2%	0.175
Definite	0.5%	0.7%	0.694
Definite/Probable	0.5%	0.7%	0.694
Timing of Event (Definite/Probable ST)			
Acute (≤ 24 hours)	0.1%	0.0%	1.000
Sub-acute (> 24 hours and ≤ 30 days)	0.2%	0.2%	1.000
Late (> 30 days and ≤ 1 year)	0.1%	0.5%	0.264

Source: Kandzari D 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, The Lancet, 2017

Subgroup Analysis: 12-month TLF

BIOFLOW-V

Subgroup	Orsiro (n = 884)	Xience (n = 450)	Favor Orsiro	Favor Xience	HR and 95% CI	p-value Interaction
Vessel Size						**0.37**
Small Vessel*	43/554 (7.8)	31/290 (10.7)			0.71 (0.45,1.13)	
Large Vessel	9/269 (3.4)	10/135 (7.4)			0.45 (0.18,1.10)	
Age						**0.16**
>75	12/124 (9.7)	6/71 (8.4)			1.20 (0.45,3.21)	
≤75	40/709 (5.6)	35/356 (9.8)			0.56 (0.35,0.88)	
Gender						**0.61**
Male	39/628 (6.2)	28/312 (9.0)			0.69 (0.42,1.11)	
Female	13/205 (6.3)	13/115 (11.3)			0.54 (0.25,1.16)	
Diabetes						**0.91**
Diabetic	18/280 (6.4)	15/153 (9.8)			0.66 (0.33, 1.31)	
Non-diabetic	34/552 (6.2)	26/273 (9.5)			0.63 (0.38,1.05)	
Lesion Length						**0.25**
>26 mm	4/78 (5.1)	6/36 (16.7)			0.31 (0.09,1.11)	
≤26 mm	48/746 (6.4)	35/387 (9.1)			0.69 (0.45,1.07)	
ACS*						**0.24**
ACS	24/426 (5.6)	23/209 (11.0)			0.50 (0.28,0.89)	
Non-ACS	28/407 (6.9)	18/218 (8.3)			0.82 (0.45,1.48)	



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Pooled Bayesian Analysis of BIOFLOW-V,-II, -IV

BIOFLOW-V

	Orsiro (n = 1,466)	Xience (n = 742)	Rate difference	Posterior	Probability
Target-lesion failure (Bayesian analysis)				Non-inferiority margin 3.85%	Superiority (post-hoc)
12-Month Rates, posterior mean ± estimate of SD (%), 95% Credible Interval (Lower, Upper)	6.3 ± 0.8 (5.0, 8.0)	8.9 ± 1.2 (6.7, 11.4)	**-2.6** ± 1.4 (-5.5, 0.1)	**100.0%**	96.9%

Bayesian analysis demonstrated unequivocal non-inferiority with a mean treatment difference of -2.6%, with 100% probability that Orsiro was non-inferior to Xience.

In a post-hoc analysis, the Bayesian posterior probability of superiority for Orsiro 12-month TLF rate vs. Xience was 96.9%.

BIOFLOW-V 24 Months - Published in Circulation

BIOFLOW-V

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Journal of the American College of Cardiology
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DOI: 10.1016/j.jacc.2018.09.019

Title:

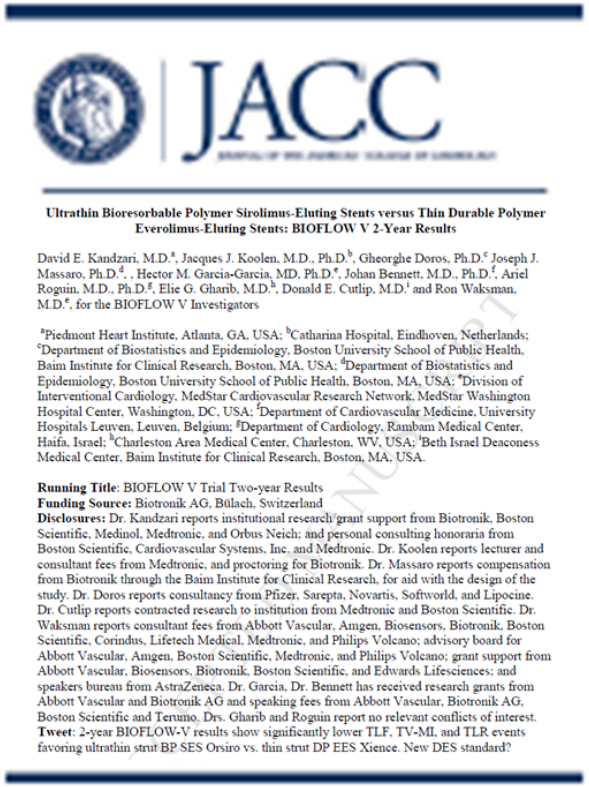
Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: BIOFLOW V 2-Year Results

Authors:

David E. Kandzari, Jacques J. Koolen, Gheorghe Doros, Joseph J. Massaro, Hector M. Garcia-Garcia, Johan Bennett, Ariel Roguin, Elie G. Gharib, Donald E. Cutlip, Ron Waksman and for the BIOFLOW V Investigators

Conclusion:

In a large randomized trial, significant differences in both TLF and target vessel-related MI persisted through 2 years favoring treatment with BP SES over DP EES. Significantly lower cumulative TLR and late/very late stent thrombosis were also observed with BP SES.



JACC

Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: BIOFLOW V 2-Year Results

David E. Kandzari, M.D.[a], Jacques J. Koolen, M.D., Ph.D.[b], Gheorghe Doros, Ph.D.[c] Joseph J. Massaro, Ph.D.[d], , Hector M. Garcia-Garcia, MD, Ph.D.[e], Johan Bennett, M.D., Ph.D.[f], Ariel Roguin, M.D., Ph.D.[g], Elie G. Gharib, M.D.[h], Donald E. Cutlip, M.D.[i] and Ron Waksman, M.D.[e], for the BIOFLOW V Investigators

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Running Title: BIOFLOW V Trial Two-year Results
Funding Source: Biotronik AG, Bülach, Switzerland
Disclosures: Dr. Kandzari reports institutional research grant support from Biotronik, Boston Scientific, Medinol, Medtronic, and Orbus Neich; and personal consulting honoraria from Boston Scientific, Cardiovascular Systems, Inc, and Medtronic. Dr. Koolen reports lecturer and consultant fees from Medtronic, and proctoring for Biotronik. Dr. Massaro reports compensation from Biotronik through the Baim Institute for Clinical Research, for aid with the design of the study. Dr. Doros reports consultancy from Pfizer, Sarepta, Novartis, Softworld, and Lipocine. Dr. Cutlip reports contracted research to institution from Medtronic and Boston Scientific. Dr. Waksman reports consultant fees from Abbott Vascular, Amgen, Biosensors, Biotronik, Boston Scientific, Corindus, Lifetech Medical, Medtronic, and Philips Volcano; advisory board for Abbott Vascular, Amgen, Boston Scientific, Medtronic, and Philips Volcano; grant support from Abbott Vascular, Biosensors, Biotronik, Boston Scientific, and Edwards Lifesciences; and speakers bureau from AstraZeneca. Dr. Garcia, Dr. Bennett has received research grants from Abbott Vascular and Biotronik AG and speaking fees from Abbott Vascular, Biotronik AG, Boston Scientific and Terumo. Drs. Gharib and Roguin report no relevant conflicts of interest.
Tweet: 2-year BIOFLOW-V results show significantly lower TLF, TV-MI, and TLR events favoring ultrathin strut BP SES Orsiro vs. thin strut DP EES Xience. New DES standard?

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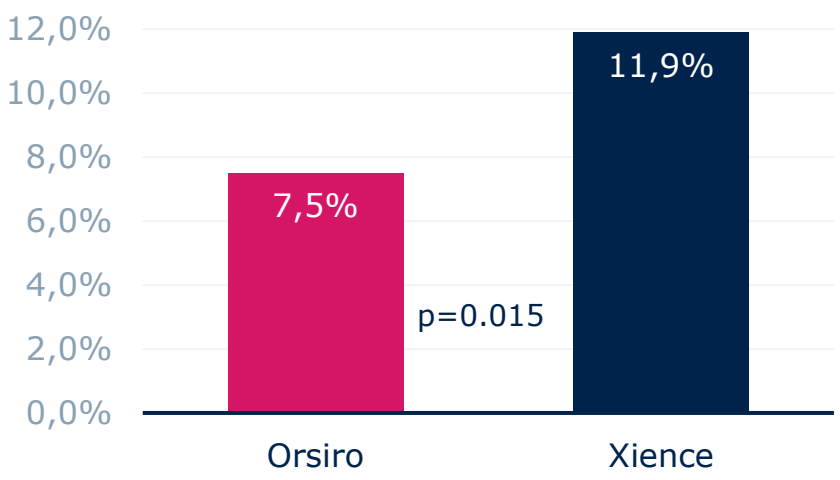
Results: 24-month Outcomes

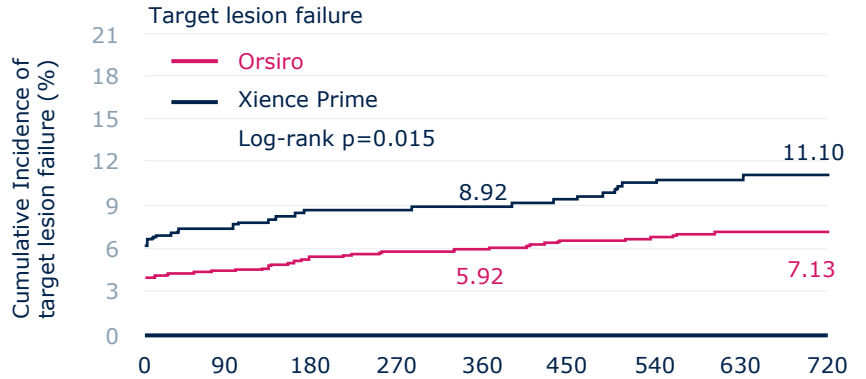
BIOFLOW-V

	Orsiro (n = 884)	Xience (n = 450)	p-value
Target lesion failure	7.5%	11.9%	0.015
Cardiac death	0.6%	0.5%	1.0
Target vessel MI	5.3%	9.5%	0.01
Clinically-driven TLR	2.6%	4.9%	0.04

TLF at 24 months



Kaplan-Meier Estimates



Number at risk

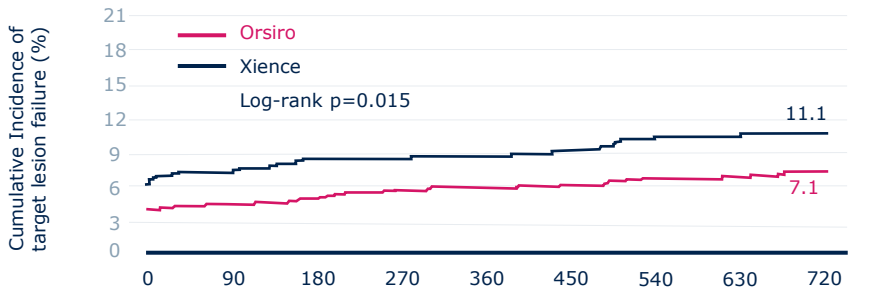
Orsiro	884	841	828	814	802	786	770	766	648
Xience Prime	450	420	411	401	394	382	374	367	306

Source: Kandzari DE et al. Journal of the American College of Cardiology. 2018 Sep 23:25565.

Results: 24-month Outcomes

BIOFLOW-V

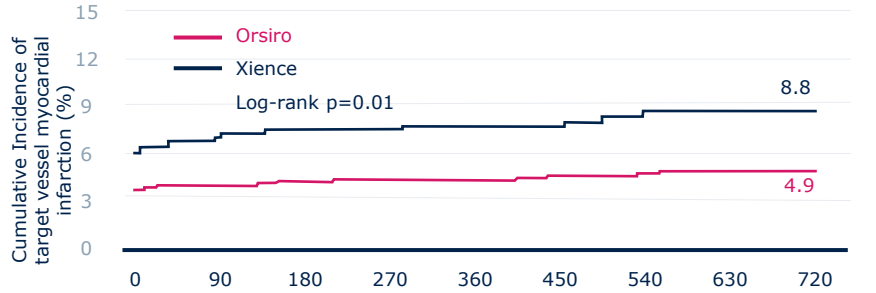
Target lesion failure



Number at risk

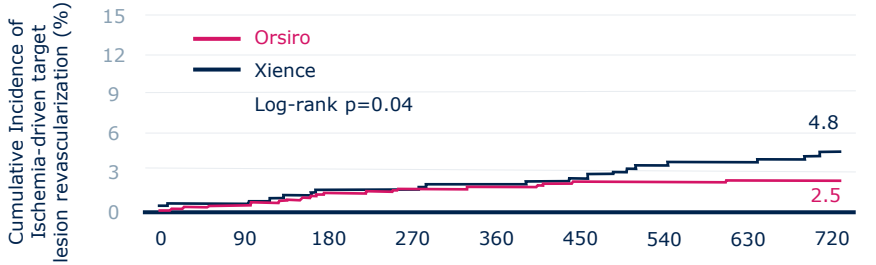
Orsiro	884	841	828	814	802	786	770	766	648
Xience Prime	450	420	411	401	394	382	374	367	306

Target vessel myocardial infarction



Orsiro	883	841	829	821	812	796	781	776	659
Xience Prime	450	420	412	404	397	385	378	373	310

Ischemia-driven target lesion revascularization

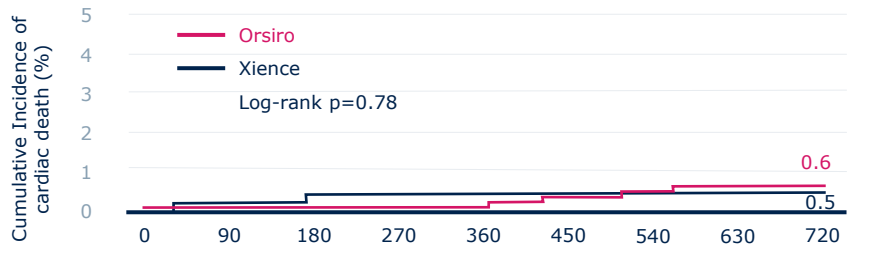


Number at risk

Orsiro	883	874	860	847	835	817	802	798	678
Xience Prime	450	445	439	429	421	407	398	392	327

Time after initial procedure (days)

Cardiac death



Orsiro	884	874	864	858	849	832	818	815	693
Xience Prime	450	447	442	437	429	416	408	407	340

Time after initial procedure (days)

Source: Kandzari DE et al. Journal of the American College of Cardiology. 2018 Sep 23:25565.

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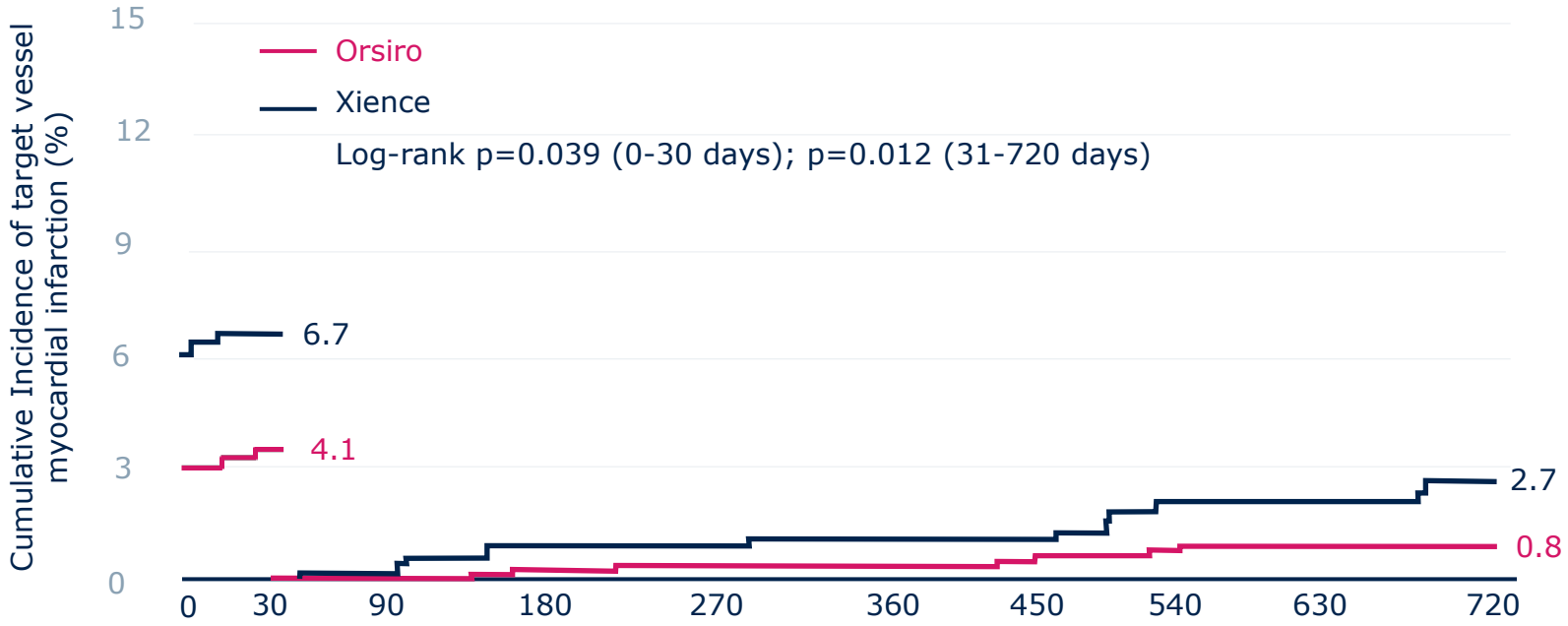
Results: 24-month Outcomes

BIOFLOW-V

Landmark Analysis TV-MI 31 days to 24 months



0-30d: Significant differences in procedural-related MI was observed favoring Orsiro.

0-720d: Through 2 years, both overall and spontaneous target-vessel-related MI event rates were significantly lower in the Orsiro cohort.

Source: Kandzari DE et al. Journal of the American College of Cardiology. 2018 Sep 23:25565.

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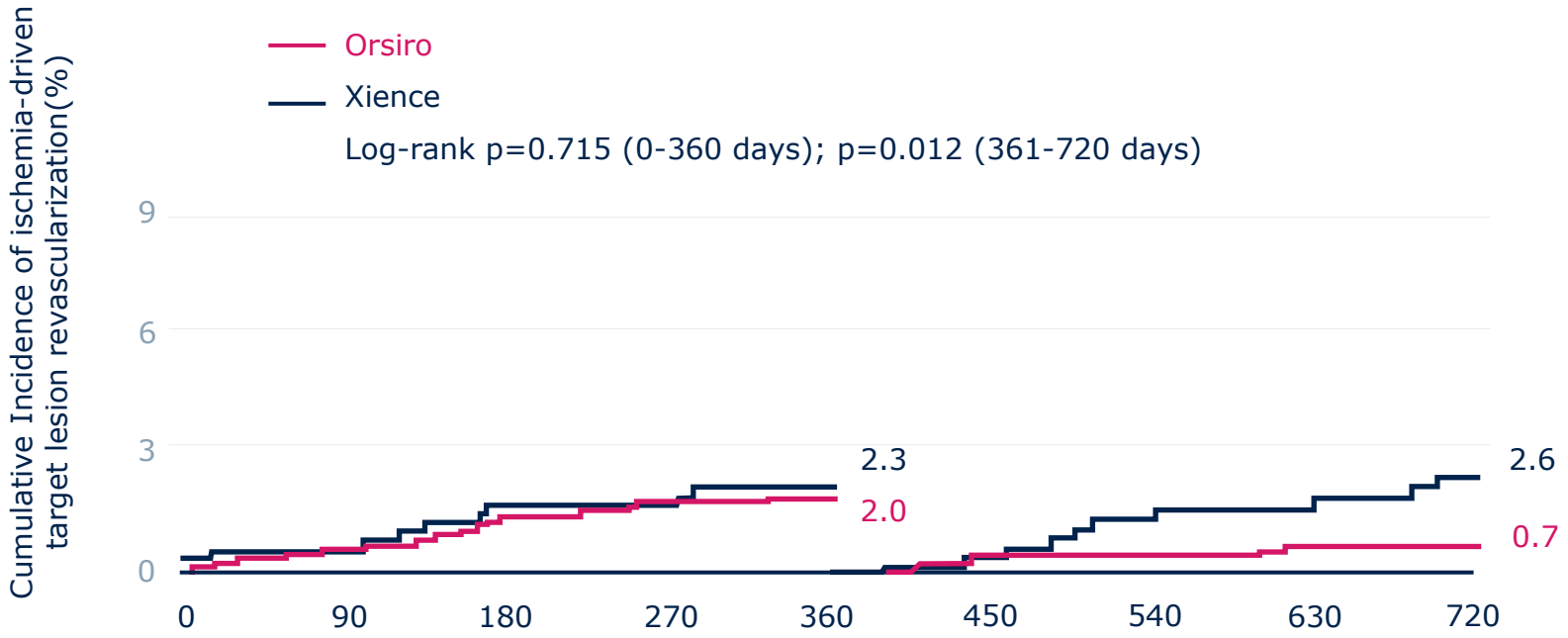
Results: 24-month Outcomes

BIOFLOW-V

Landmark Analysis ischemia-driven Target Lesion Revascularization 12 months to 24 months



A lower rate of repeat TLR through 2 years was observed with Orsiro. Notably, rates of ischemia-driven TLR at 1 year were similar between stent groups, yet a significant difference in late TLR beyond 1 year favoring Orsiro emerged. The finding aligns with other clinical study results (BIO-RESORT).

Source: Kandzari DE et al. Journal of the American College of Cardiology. 2018 Sep 23:25565.

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Results: 24-month Outcomes

BIOFLOW-V

Stent Thrombosis Events	Orsiro (n = 884)	Xience (n = 450)	P Value
Definite	0.5%	1.2%	0.17
Probable	0	0	---
Any ARC (Definite/Probable/Possible)	0.7%	1.5%	0.23
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 ≤2 years)	0	0.5%	0.11
Late/Very Late (>30 days ≤2 years)	0.1%	1.0%	**0.045**

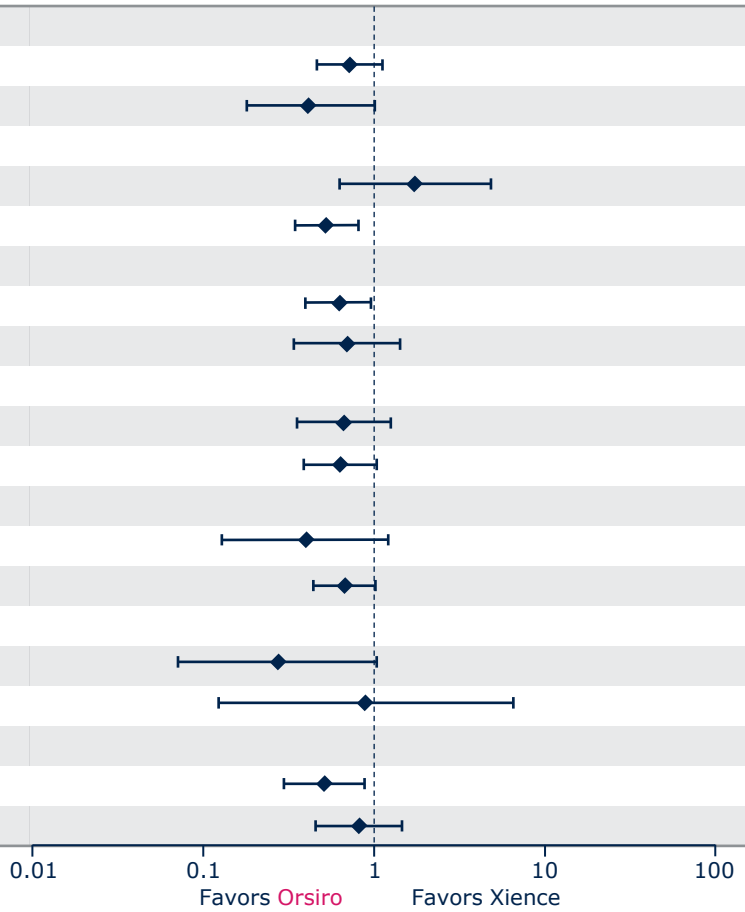
DAPT adherence at 2 years: 45.6% (368/807) Orsiro; 45.1% (181/401) Xience; P = 0.94

Source: Kandzari DE et al. Journal of the American College of Cardiology. 2018 Sep 23:25565.

Target Lesion Failure at 24 Months by Subgroups

BIOFLOW-V

Subgroups	HR and 95% CI	p Value for Interaction
Vessel Size		0.242
Small Vessels	0.72 (0.47, 1.10)	
Large Vessels	0.42 (0.19, 0.94)	
Age		**0.039**
>75	1.70 (0.61, 4.71)	
≤75	0.53 (0.35, 0.79)	
Gender		0.791
Male	0.62 (0.40, 0.96)	
Female	0.69 (0.34, 1.38)	
Diabetes		0.844
Diabetic	0.66 (0.36, 1.24)	
Non-diabetic	0.62 (0.39, 0.99)	
Lesion Length		0.371
>26 mm	0.39 (0.13, 1.16)	
≤26 mm	0.67 (0.45, 1.00)	
Overlapping		0.349
Non-overlapping	0.27 (0.07, 1.02)	
Overlapping	0.88 (0.12, 6.23)	
ACS		0.259
ACS	0.51 (0.31, 0.86)	
Non-ACS	0.80 (0.46, 1.38)	



Source: Kandzari DE et al. Journal of the American College of Cardiology. 2018 Sep 23:25565.

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Multivariable Analysis of TLF, TV-MI and TLR at 24 Months

BIOFLOW-V

	Odds Ratio (95% Confidence Interval)	P value
TLF at 2 Years		
BP SES vs. DP EES	0.64 (0.42, 0.95)	0.03
Subjects with Two Vessels Treated	1.64 (0.79, 3.38)	0.18
Number of Stents Implanted (per patient)	1.23 (0.78, 1.94)	0.37
Total Stent Lengths (mm) (sum per patient)	1.01 (0.98, 1.03)	0.59
Number of Target Lesions (per patients)	0.95 (0.52, 1.73)	0.86
Target Vessel-Related MI at 2 Years		
History of MI	1.86 (1.16, 3.00)	0.01
BP SES vs. DP EES	0.56 (0.35, 0.88)	0.01
Subjects with Two Vessels Treated	1.89 (0.84, 4.25)	0.12
Subjects with Overlapping Stents vs. without	1.60 (0.70, 3.65)	0.26
Number of Target Lesions (per patient)	1.22 (0.56, 2.64)	0.62
Number of Stents Implanted (per patient)	1.05 (0.55, 2.03)	0.88
Total Stent Lengths (mm) (sum per patient)	1.00 (0.98, 1.02)	0.96
Ischemia Driven TLR at 2 Years		
History of CABG	4.42 (1.86, 10.51)	<0.001
Unstable Angina vs. Stable Angina	2.16 (1.06, 4.43)	0.035
BP SES vs. DP EES	0.55 (0.28, 1.08)	0.08
Hypertension	2.83 (0.85, 9.41)	0.09
Subjects with Two Vessels Treated	1.91 (0.60, 6.10)	0.27
Number of Stent Implanted (per patient)	1.28 (0.67, 2.42)	0.455
Documented Silent Ischemia vs. Stable Angina	1.42 (0.45, 4.50)	0.55
Total Stent Lengths (mm) (sum per patient)	1.01 (0.97, 1.04)	0.74
Number of Target Lesions (per patient)	0.97 (0.40, 2.33)	0.945

Source: Kandzari DE et al. Journal of the American College of Cardiology. 2018 Sep 23:25565.

Conclusions

BIOFLOW-V

1. At 1 year Bayesian pooled analysis including patient level outcomes from BIOFLOW-II and -IV trial demonstrated unequivocal non-inferiority with mean TLF treatment difference of -2.6% favoring Orsiro and posterior probability of superiority 96.9%

2. Through 2 years significant differences in TLF and target vessel MI observed at 1 year were maintained in addition to emergence of other safety and efficacy differences that favor Orsiro over a contemporary generation thin strut DP EES
   - Lower TLF (7.5% vs 11.9%, P = 0.015)
   - Lower target vessel related MI (5.3% vs 9.5%, P = 0.01), both early (<30 days) and late (30 days to 2 years)
   - Lower ischemia-driven TLR, driven by differences in late (>1 year) TLR (2.6% vs 4.9%, P = 0.04)
   - Lower late/very late definite/probable ST (0.1% vs 1.0%, P = 0.045)

3. These results not only advance a standard of comparison for new DES but also direct attention to strut thickness and polymer composition as key features for iterative DES development

Source: Kandzari D, BIOFLOW V Comparison of UltraThin Sirolimus-Eluting Bioresorbable Polymer with Thin Everolimus- Eluting Durable Polymer Stents, Oral presentation ESC 2017; Kandzari D, Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents in Patients Undergoing Coronary Revascularization: Two-year Outcomes from the Randomized BIOFLOW V Trial, Oral presentation tct2018

BIOFLOW-V 36 Months - Published in Circulation

BIOFLOW-V

Publication:

Journal of the American College of Cardiology
Published Online June, 2020
DOI: 10.1016/j.jcin.2020.02.019

Title:

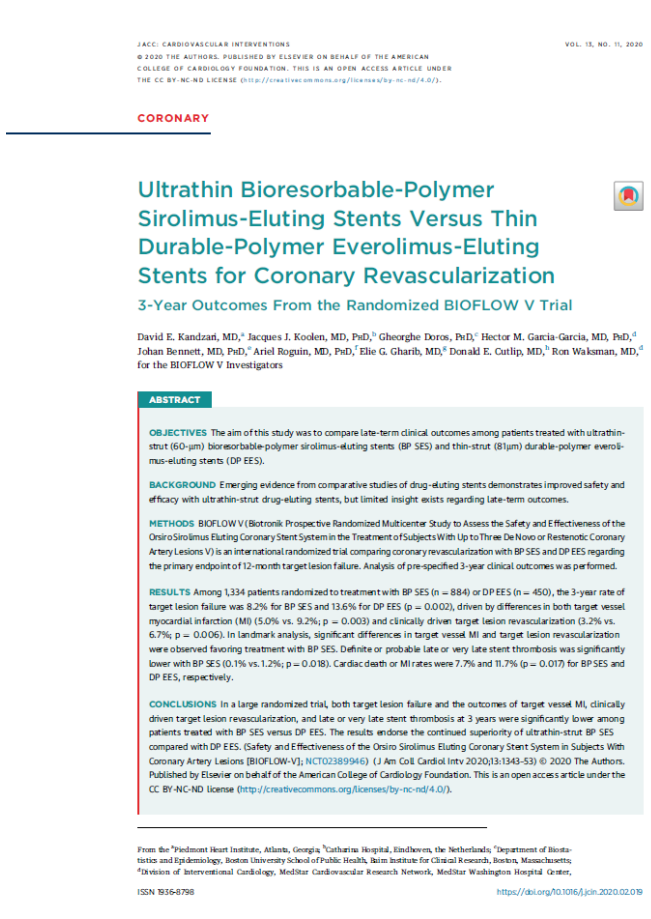
Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: BIOFLOW V 3-Year Results

Authors:

David E. Kandzari, Jacques J. Koolen, Gheorghe Doros, Joseph J. Massaro, Hector M. Garcia-Garcia, Johan Bennett, Ariel Roguin, Elie G. Gharib, Donald E. Cutlip, Ron Waksman and for the BIOFLOW V Investigators

Conclusion:

In a large randomized trial, both target lesion failure and the outcomes of target vessel MI, clinically driven target lesion revascularization, and late or very late stent thrombosis at 3 years were significantly lower among patients treated with BP SES versus DP EES. The results endorse the continued superiority of ultrathin-strut BP SES compared with DP EES.



JACC: CARDIOVASCULAR INTERVENTIONS VOL. 13, NO. 11, 2020

CORONARY

Ultrathin Bioresorbable-Polymer Sirolimus-Eluting Stents Versus Thin Durable-Polymer Everolimus-Eluting Stents for Coronary Revascularization

3-Year Outcomes From the Randomized BIOFLOW V Trial

David E. Kandzari, MD,[a] Jacques J. Koolen, MD, PhD,[b] Gheorghe Doros, PhD,[c] Hector M. Garcia-Garcia, MD, PhD,[d] Johan Bennett, MD, PhD,[e] Ariel Roguin, MD, PhD,[f] Elie G. Gharib, MD,[g] Donald E. Cutlip, MD,[h] Ron Waksman, MD,[d] for the BIOFLOW V Investigators

ABSTRACT

OBJECTIVES The aim of this study was to compare late-term clinical outcomes among patients treated with ultrathin-strut (60-μm) bioresorbable-polymer sirolimus-eluting stents (BP SES) and thin-strut (81μm) durable-polymer everolimus-eluting stents (DP EES).

BACKGROUND Emerging evidence from comparative studies of drug-eluting stents demonstrates improved safety and efficacy with ultrathin-strut drug-eluting stents, but limited insight exists regarding late-term outcomes.

METHODS BIOFLOW V (Biotronik Prospective Randomized Multicenter Study to Assess the Safety and Effectiveness of the Orsiro Sirolimus Eluting Coronary Stent System in the Treatment of Subjects With Up to Three De Novo or Restenotic Coronary Artery Lesions V) is an international randomized trial comparing coronary revascularization with BP SES and DP EES regarding the primary endpoint of 12-month target lesion failure. Analysis of pre-specified 3-year clinical outcomes was performed.

RESULTS Among 1,334 patients randomized to treatment with BP SES (n = 884) or DP EES (n = 450), the 3-year rate of target lesion failure was 8.2% for BP SES and 13.6% for DP EES (p = 0.002), driven by differences in both target vessel myocardial infarction (MI) (5.0% vs. 9.2%; p = 0.003) and clinically driven target lesion revascularization (3.2% vs. 6.7%; p = 0.006). In landmark analysis, significant differences in target vessel MI and target lesion revascularization were observed favoring treatment with BP SES. Definite or probable late or very late stent thrombosis was significantly lower with BP SES (0.1% vs. 1.2%; p = 0.018). Cardiac death or MI rates were 7.7% and 11.7% (p = 0.017) for BP SES and DP EES, respectively.

CONCLUSIONS In a large randomized trial, both target lesion failure and the outcomes of target vessel MI, clinically driven target lesion revascularization, and late or very late stent thrombosis at 3 years were significantly lower among patients treated with BP SES versus DP EES. The results endorse the continued superiority of ultrathin-strut BP SES compared with DP EES. (Safety and Effectiveness of the Orsiro Sirolimus Eluting Coronary Stent System in Subjects With Coronary Artery Lesions [BIOFLOW-V]; NCT02389946) (J Am Coll Cardiol Intv 2020;13:1343-53) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]Piedmont Heart Institute, Atlanta, Georgia; [b]Catharina Hospital, Eindhoven, the Netherlands; [c]Department of Biostatistics and Epidemiology, Boston University School of Public Health, Baim Institute for Clinical Research, Boston, Massachusetts; [d]Division of Interventional Cardiology, MedStar Cardiovascular Research Network, MedStar Washington Hospital Center,

ISSN 1936-8798 https://doi.org/10.1016/j.jcin.2020.02.019

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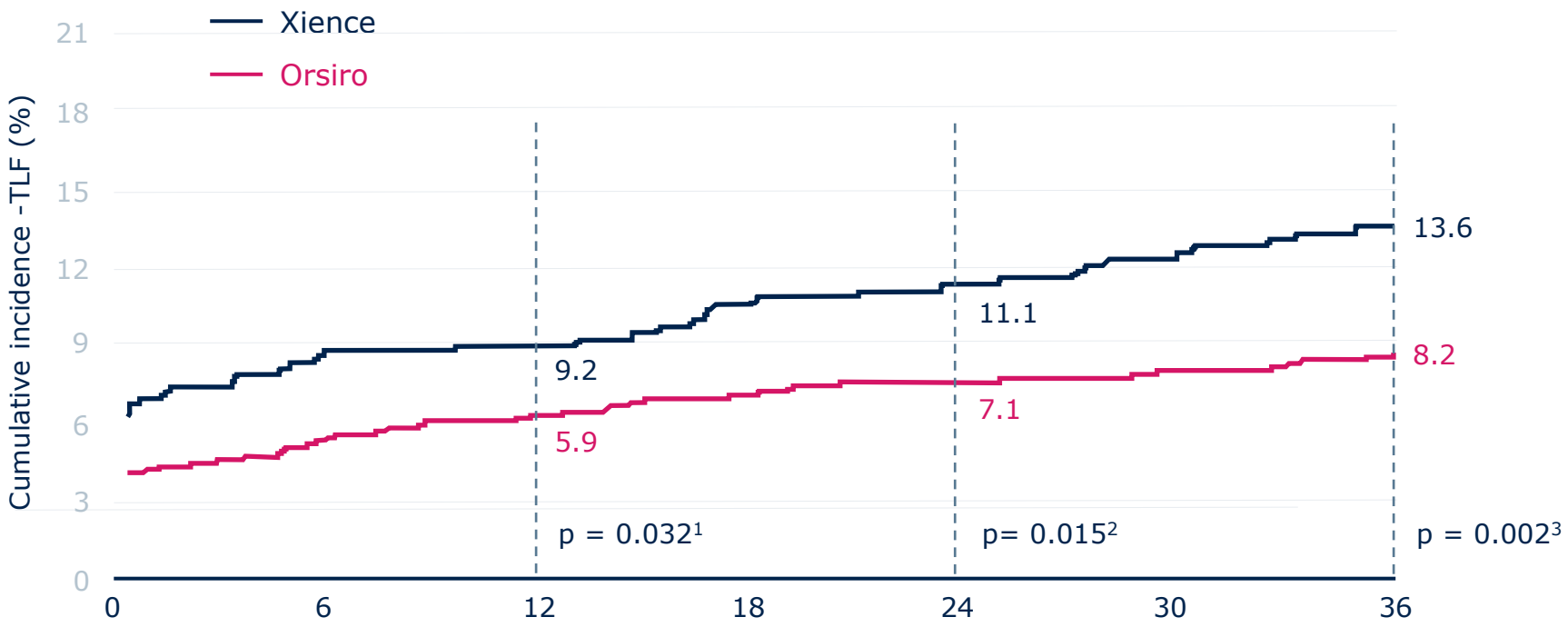
Target Lesion Failure at 36 Months

BIOFLOW-V

TLF out to 36 months



Source: 1. Kandzari D 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 Oct 21; 390(10105):1843-1852; 2. Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: Journal of American College of Cardiology (2018), doi: https//doi.org/10.1016/j.jacc.2018.09.019;
3. Kandzari D et al. J Am Coll Cardiol. Cardiovasc Interven. 2020, doi: 10.1016/j.jcin.2020.02.019.

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Clinical Outcomes at 36 Months

BIOFLOW-V

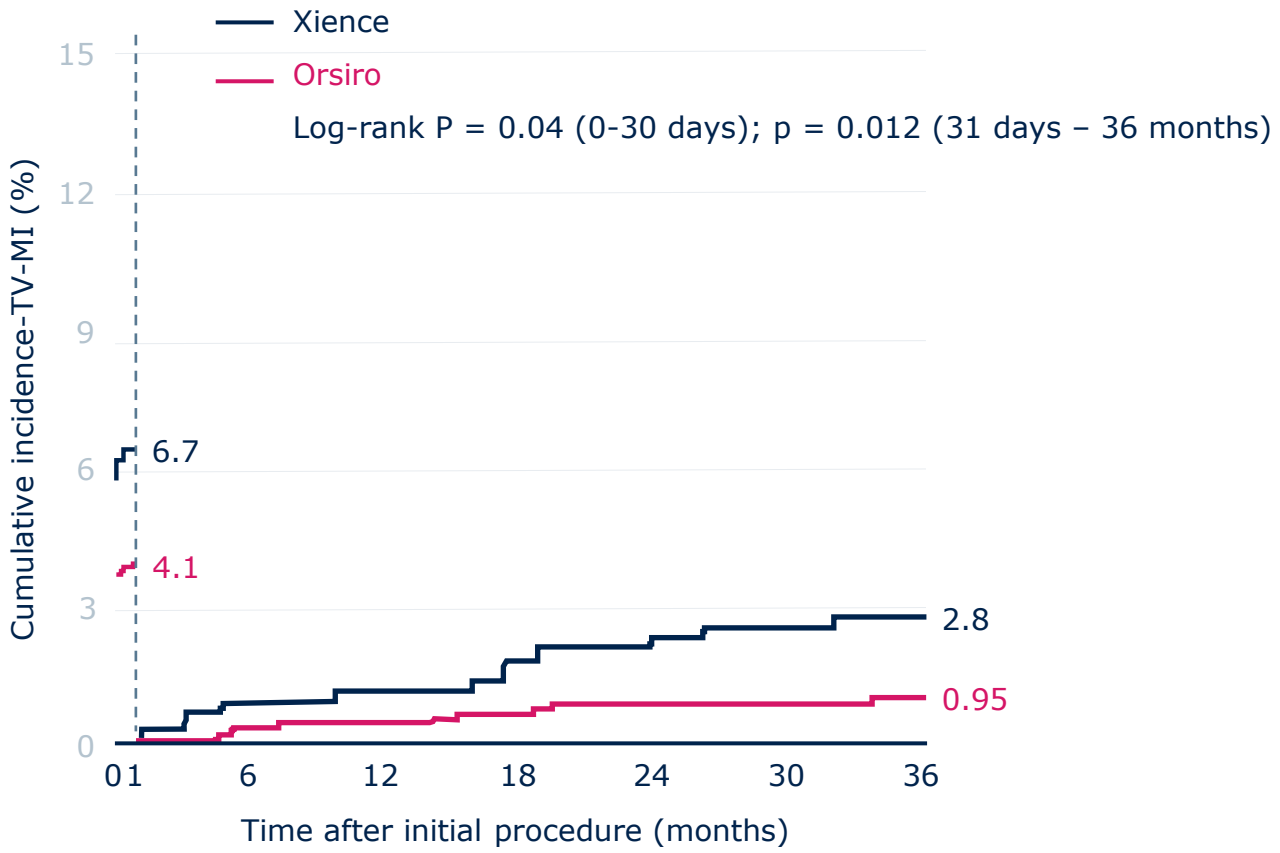
	Orsiro (n = 884)	Xience (n = 450)	Difference [95% Confidence Interval]	P value
Target lesion failure	**8.6% (70/814)**	**14.4% (59/411)**	**-5.76% [-9.86%, -2.03%]**	**0.003**
Cardiac death	1.1% (9/807)	1.2% (5/408)	-0.11% [-1.81%, 1.10%]	1.00
Target vessel myocardial infarction	5.5% (44/804)	10.1% (40/406)	-4.63% [-8.21%, -1.49%]	**0.004**
Ischemia-driven target lesion revascularization	3.4% (27/804)	6.9% (28/404)	-3.57% [-6.66%, -1.01%]	**0.008**
All-cause death	3.2% (26/824)	4.0.% (17/420)	-0.89% [-3.43%, 1.18%]	0.416
Cardiac death or any MI	8.1% (66/813)	12.4% (51/410)	-4.32% [-8.25%, -0.79%]	**0.018**
MACE	11.9% (99/831)	18.0% (76/422)	-6.10% [-10.54%, -1.97%]	**0.004**
Target vessel failure	10.2% (83/814)	17.0% (70/412)	-6.79% [-11.15%, -2.77%]	**<0.001**
Ishchemia-driven target vessel revascularization	5.6% (45/804)	10.4% (42/405)	-4.77% [-8.40%, -1.60%]	**0.003**

Source: Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: BIOFLOW V 3-Year Results J Am Coll Cardiol. Cardiovasc Interven. 2020, doi: 10.1016/j.jcin.2020.02.019.

Clinical Outcomes at 36 Months

BIOFLOW-V

Landmark analysis target vessel myocardial infarction (TV-MI)

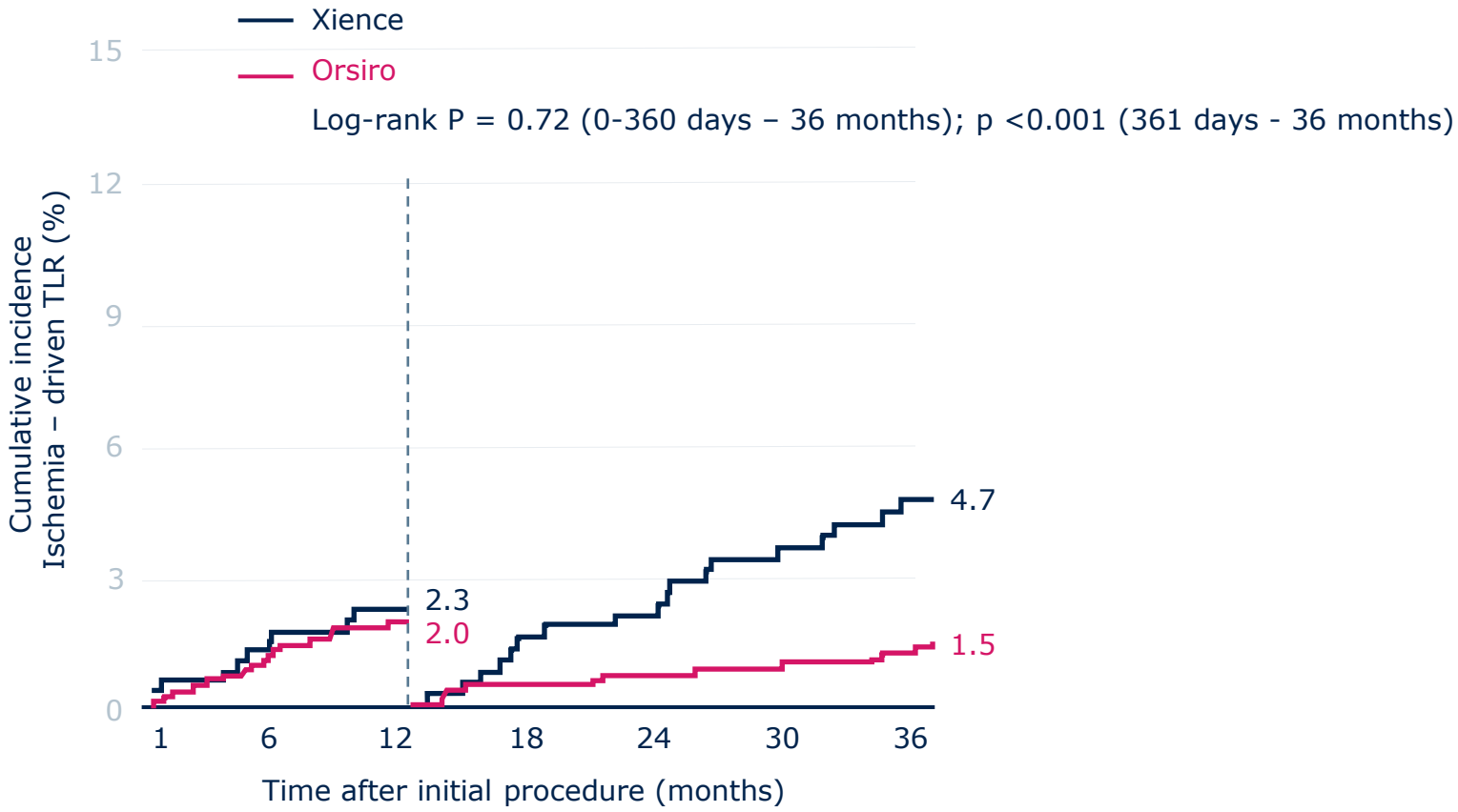


Source: Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: BIOFLOW V 3-Year Results, J Am Coll Cardiol. Cardiovasc Interven. 2020, doi: 10.1016/j.jcin.2020.02.019.

Clinical Outcomes at 36 Months

BIOFLOW-V

Landmark analysis ischemia-driven target lesion revascularization (ischemia-driven TLR)



Source: Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: BIOFLOW V 3-Year Results, J Am Coll Cardiol. Cardiovasc Interven. 2020, doi: 10.1016/j.jcin.2020.02.019.

Stent Thrombosis Rates at 36 Months

BIOFLOW-V

	Orsiro (n = 884)	Xience (n = 450)	Difference [95% Confidence Interval]	P value
Definite stent thrombosis	**0.5% (4/801)**	**1.5% (6/403)**	**-0.99% [-2.74%, 0.13%]**	**0.094**
Probable stent thrombosis	0.0% (0/799)	0.0% (0/403)	0.00% [-0.94%, 0.48%]	-
Definite/probable stent thrombosis	**0.5% (4/801)**	**1.5% (6/403)**	**-0.99% [-2.74%, 0.13%]**	**0.094**
Early	0.3% (3/878)	0.2% (1/449)	0.12% [-0.93%, 0.80%]	1.00
Acute (<=24 hours)	0.1% (1/884)	0.0% (0/450)	0.11% [-0.74%, 0.64%]	1.00
Sub-acute (> 24 hours and <=30 days)	0.2% (2/878)	0.2% (1/449)	0.01% [-1.04%, 0.63%]	1.00
Late (> 30 days and <=1 year)	0.1% (1/799)	0.5% (2/403)	-0.37% [-1.67%, 0.31%]	0.26
Very late (> 1 year and <=3 years)	0.0% (0/799)	0.7% (3/403)	-0.74% [-2.17%, 0.06%]	**0.038**
Any late/very late ST	0.6% (5/802)	1.7% (7/405)	-1.10% [-2.94%, 0.11%]	0.119
Definite late/very late ST	0.1% (1/799)	1.2% (5/403)	-1.12% [-2.75%, -0.20%]	**0.018**
Possible late/very late ST	0.5% (4/802)	0.5% (2/405)	0.00% [-1.32%, 0.86%]	1.00
Probable late/very late ST	0.0% (0/799)	0.0% (0/403)	-0.00% [-0.94%, 0.48%]	-
Definite/probable late/very late ST	0.1% (1/799)	1.2% (5/403)	-1.12% [-2.75%, -0.20%]	**0.018**

Source: Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: BIOFLOW V 3-Year Results, J Am Coll Cardiol. Cardiovasc Interven. 2020, doi: 10.1016/j.jcin.2020.02.019.

BIOFLOW-V 60 Months – Submitted to JACC

BIOFLOW-V

Submitted publication:
Journal of the American College of Cardiology, 2022, NCT02389946

Outcomes presented at CRT 2022

Title:
Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents for Coronary Revascularization: Final 5-year Outcomes from the Randomized BIOFLOW V Trial

Authors:
David E. Kandzari, Jacques J. Koolen, Gheorghe Doros, Joseph J. Massaro, Hector M. Garcia-Garcia, Johan Bennett, Ariel Roguin, Elie G. Gharib, Donald E. Cutlip, Ron Waksman and for the BIOFLOW V Investigators

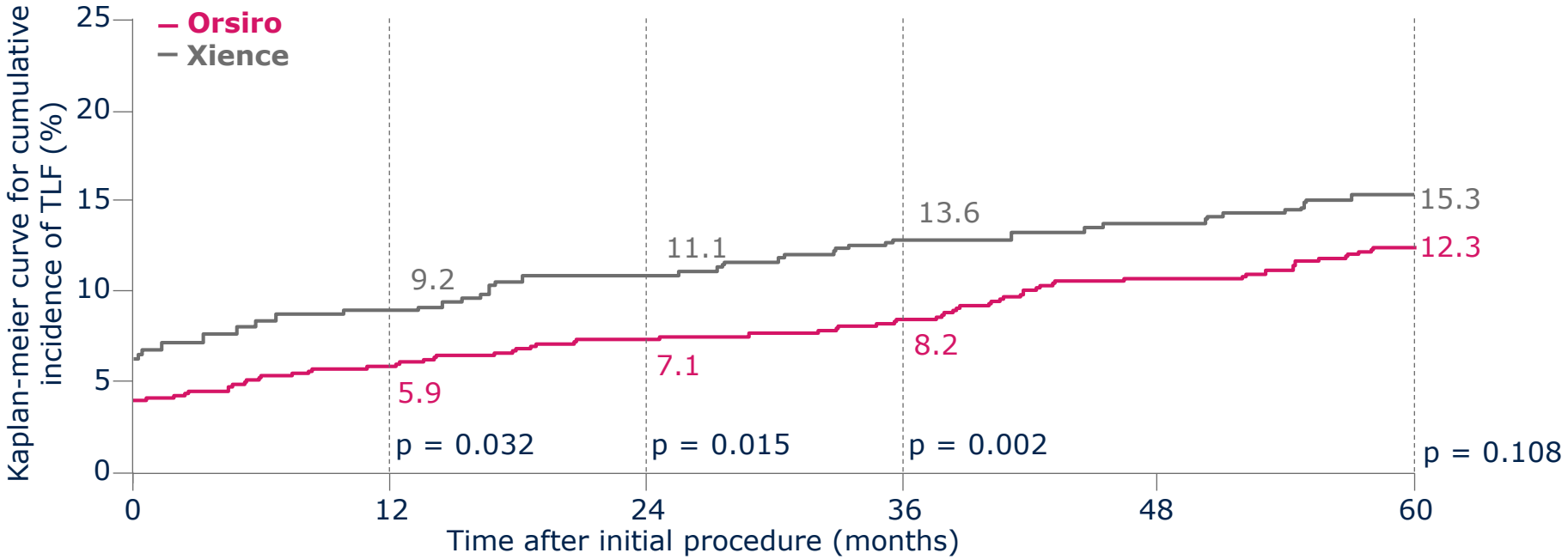
Conclusion:
In a large, randomized trial, TLF and the individual outcomes of cardiac death and TLR at 5-years were similar among patients treated with BP SES versus DP EES. Both TV MI and late/very late definite/probable stent thrombosis were significantly lower with BP SES. These results confirm the durability of safety and effectiveness of PCI with ultrathin BP SES.

Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents for Coronary Revascularization: Final 5-year Outcomes from the Randomized BIOFLOW V Trial, Submitted manuscript to JACC:2022 NCT02389946. All figures from submitted manuscript are rounded by Biotronik after the BIOFLOW-V figures presented by D. Kandzari, at CRT 2022, Washington, USA.

Primary Endpoint - Target Lesion Failure at 60 Months

BIOFLOW-V

Target lesion failure at 60 months[1,2,3,4]



Number at risk

Orsiro	884	834	794	765	739	504
Xience	450	413	386	369	354	240

1. Kandzari D 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 Oct 21; 390(10105):1843-1852; 2. Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: Journal of American College of Cardiology (2018), doi: https//doi.org/10.1016/j.jacc.2018.09.019; 3. Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents: BIOFLOW V 3-Year Results, J Am Coll Cardiol. Cardiovasc Interven. 2020, doi: 10.1016/j.jcin.2020.02.019. 4.Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents for Coronary Revascularization: Final 5-year Outcomes from the Randomized BIOFLOW V Trial, Submitted manuscript to JACC:2022 NCT02389946. All figures from submitted manuscript are rounded by Biotronik after the BIOFLOW-V figures presented by D. Kandzari, at CRT 2022, Washington, USA.

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Clinical Outcomes at 60 Months

BIOFLOW-V

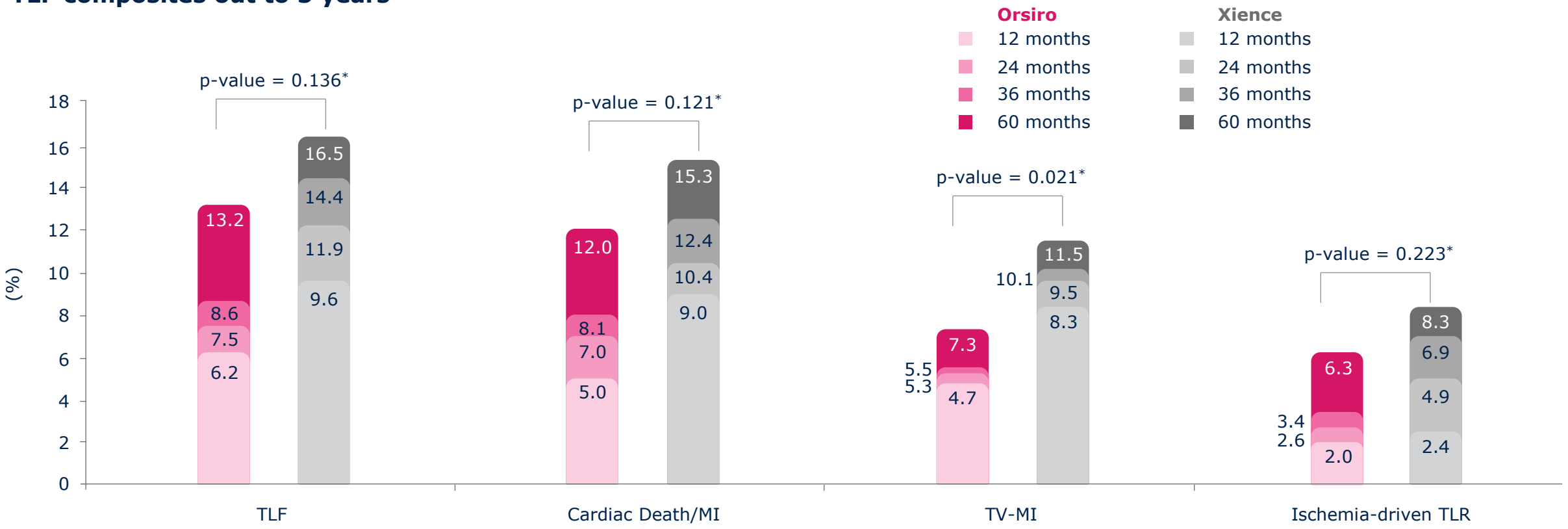
	Orsiro (n = 884)	Xience (n = 450)	Difference [95% Confidence Interval]	P value
Target lesion failure	**13.2% (104/787)**	**16.5% (66/399)**	**-3.33% [-7.85%, 0.86%]**	**0.136**
Cardiac death	2.7% (21/774)	2.0% (8/392)	0.67% [-1.47%, 2.39%]	0.555
Target vessel myocardial infarction	7.3% (56/765)	11.5% (45/391)	-4.19% [-8.09%, -0.71%]	**0.021**
Ischemia-driven target lesion revascularization	6.3% (48/761)	8.3% (32/388)	-1.94% [-5.45%, 1.11%]	0.223
All-cause death	6.9% (56/808)	6.6% (27/411)	0.36% [-2.86%, 3.17%]	0.904
Cardiac death or any MI	12.0% (94/786)	15.3% (61/398)	-3.37% [-7.76%, 0.67%]	0.121
MACE	18.9% (155/820)	22.1% (92/416)	-3.21% [-8.15%, 1.46%]	0.201
Target vessel failure	16.1% (127/788)	20.2% (81/401)	-4.08% [-8.92%, 0.47%]	0.090
Ishchemia-driven target vessel revascularization	10.2% (78/763)	13.1% (51/390)	-2.85% [-7.05%, 0.95%]	0.167

Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents for Coronary Revascularization: Final 5-year Outcomes from the Randomized BIOFLOW V Trial, Submitted manuscript to JACC:2022 NCT02389946.

Clinical Outcomes up to 60 Months

BIOFLOW-V

TLF composites out to 5 years[1-5]



*Frequentist analysis

Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents for Coronary Revascularization: Final 5-year Outcomes from the Randomized BIOFLOW V Trial, Submitted manuscript to JACC:2022 NCT02389946. All figures from submitted manuscript are rounded by Biotronik after the BIOFLOW-V figures presented by D. Kandzari, at CRT 2022, Washington, USA.

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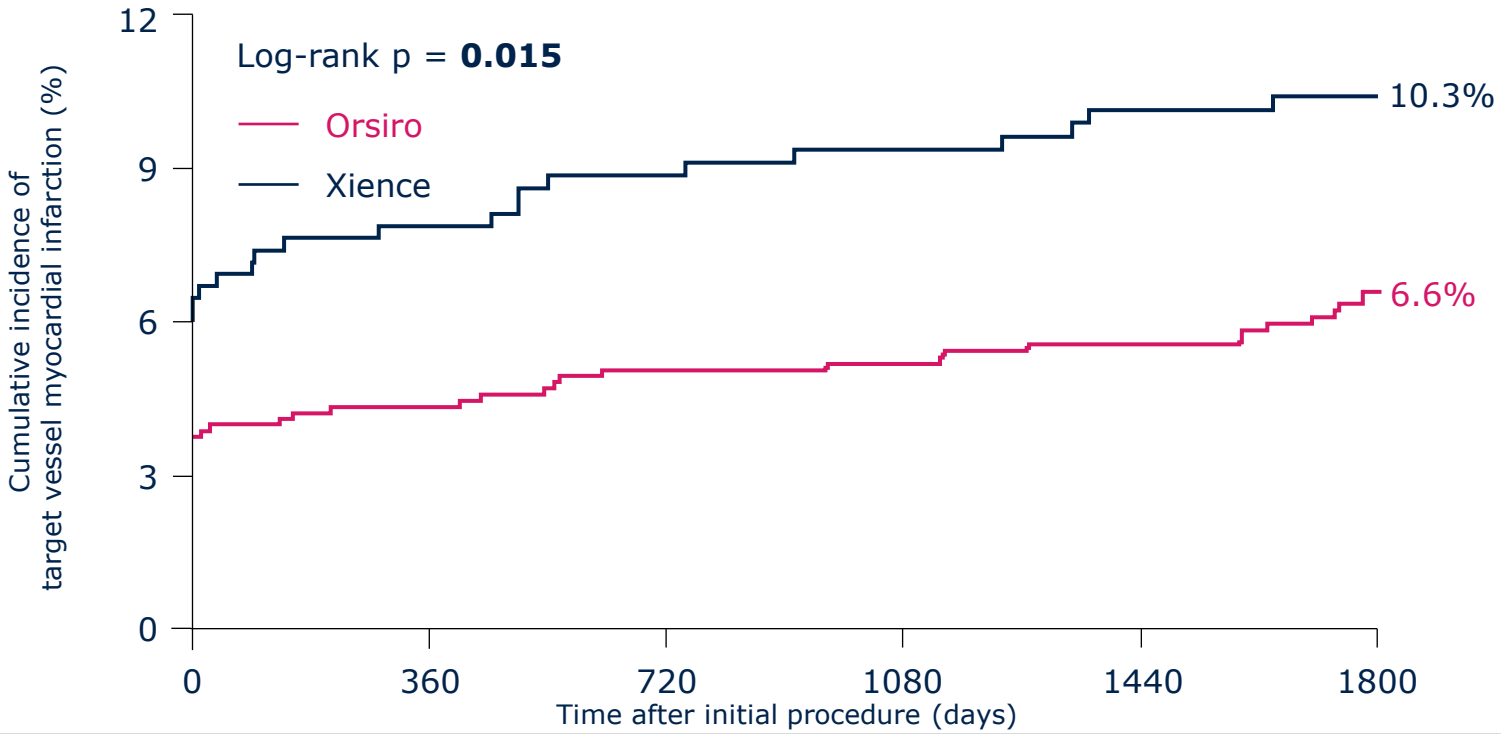
Clinical Outcomes at 60 Months

BIOFLOW-V

Target vessel myocardial infarction at 60 months



Number at risk

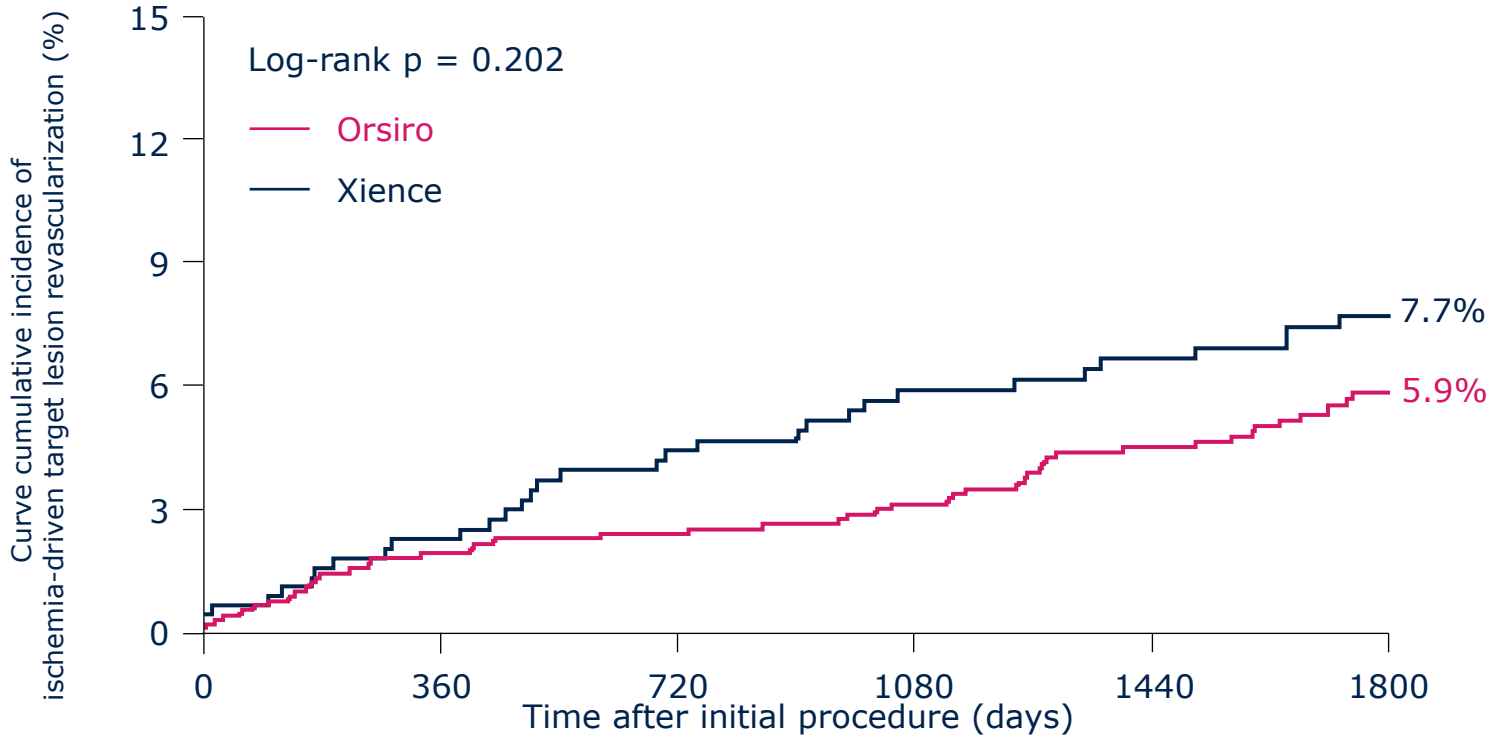
Orsiro	883	834	802	775	749	514
Xience	450	413	389	374	364	246

Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents for Coronary Revascularization: Final 5-year Outcomes from the Randomized BIOFLOW V Trial, Submitted manuscript to JACC:2022 NCT02389946. All figures from submitted manuscript are rounded by Biotronik after the BIOFLOW-V figures presented by D. Kandzari, at CRT 2022, Washington, USA.

Clinical Outcomes at 60 Months

BIOFLOW-V

Ischemia driven target lesion revascularisation at 60 months



Number at risk

Orsiro	883	866	824	799	769	524
Xience	450	437	412	392	377	254

Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents for Coronary Revascularization: Final 5-year Outcomes from the Randomized BIOFLOW V Trial, Submitted manuscript to JACC:2022 NCT02389946. All figures from submitted manuscript are rounded by Biotronik after the BIOFLOW-V figures presented by D. Kandzari, at CRT 2022, Washington, USA.

Stent thrombosis at 60 Months

BIOFLOW-V

	Orsiro (n = 884)	Xience (n = 450)	Difference [95% Confidence Interval]	P value
Definite stent thrombosis	0.7% (5/756)	1.8% (7/385)	-1.16% [-3.08%, 0.13%]	0.120
Probable stent thrombosis	0.0% (0/753)	0.0% (0/384)	0.00% [-0.99%, 0.51%]	---
Definite/probable stent thrombosis	**0.7% (5/756)**	**1.8% (7/385)**	**-1.16% [-3.08%, 0.13%]**	**0.120**
Early	0.3% (3/879)	0.2% (1/449)	0.12% [-0.93%, 0.80%]	1.000
Acute (<=24 hours)	0.1% (1/884)	0.0% (0/450)	0.11% [-0.74%, 0.64%]	1.000
Sub-acute (> 24 hours and <=30 days)	0.2% (2/879)	0.2% (1/449)	0.00% [-1.04%, 0.63%]	1.000
Late (> 30 days and <=1 year)	0.1% (1/753)	0.5% (2/384)	-0.39% [-1.75%, 0.33%]	0.265
Very late (> 1 year and <=3 years)	0.1% (1/753)	1.0% (4/384)	-0.91% [-2.52%, -0.02%]	**0.047**
Any late/very late ST	1.7% (13/764)	3.1% (12/390)	-1.38% [-3.71%, 0.39%]	0.138
Definite late/very late ST	0.3% (2/753)	1.6% (6/384)	-1.30% [-3.11%, -0.20%]	**0.021**
Probable late/very late ST	0.0% (0/753)	0.0% (0/384)	0.00% [-0.99%, 0.51%]	--
Definite/probable late/very late ST	0.3% (2/753)	1.6% (6/384)	-1.30% [-3.11%, -0.20%]	**0.021**

Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents for Coronary Revascularization: Final 5-year Outcomes from the Randomized BIOFLOW V Trial, Submitted manuscript to JACC:2022 NCT02389946.

Conclusions

BIOFLOW-V

1

Orsiro outperformed Xience at 1-year and sustained performance up to 5 years:

- 20% lower Target Lesion Failure (13.2% vs. 16.5%, p = 0.136)
- **36% significantly lower Target Vessel Myocardial Infarction (7.3% vs. 11.5%, p = 0.021)**
- 23% lower Ischemia-Driven TLR (6.3% vs. 8.3%, p = 0.223)
- 22% lower Cardiac Death/Myocardial Infarction (12% vs. 15.3%, p = 0.121)

2

Orsiro showed a 0.7% definite/probable stent thrombosis rate overall through 5 years: 64% lower compared to Xience (0.7% vs. 1.8%, p=0.120).

Orsiro showed **83% significantly less late/very late definite/probable stent thrombosis (0.3% vs. 1.6%, p = 0.021)**

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