Bioflow-DAPT

Biodegradable-Polymer or Durable-Polymer Stents in Patients at High Bleeding Risk

A randomized, open-label clinical trial to assess the safety of HBR patients undergoing PCI with implantation of a drug-eluting stent and treated with DAPT for 1 month

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Declaration conflict of interest

- Grants and/or personal fees from Astra Zeneca, Terumo, Alvimedica/CID, Abbott Vascular, Daiichi Sankyo, Bayer, CoreFLOW, Idorsia Pharmaceuticals-Ltd, Universität Basel Department Klinische Forschung, Vifor, Bristol-Myers-Squib SA, Biotronik, Boston scientific, Medtronic, Vesalio, Novartis, Chiesi, PhaseBio.

Background

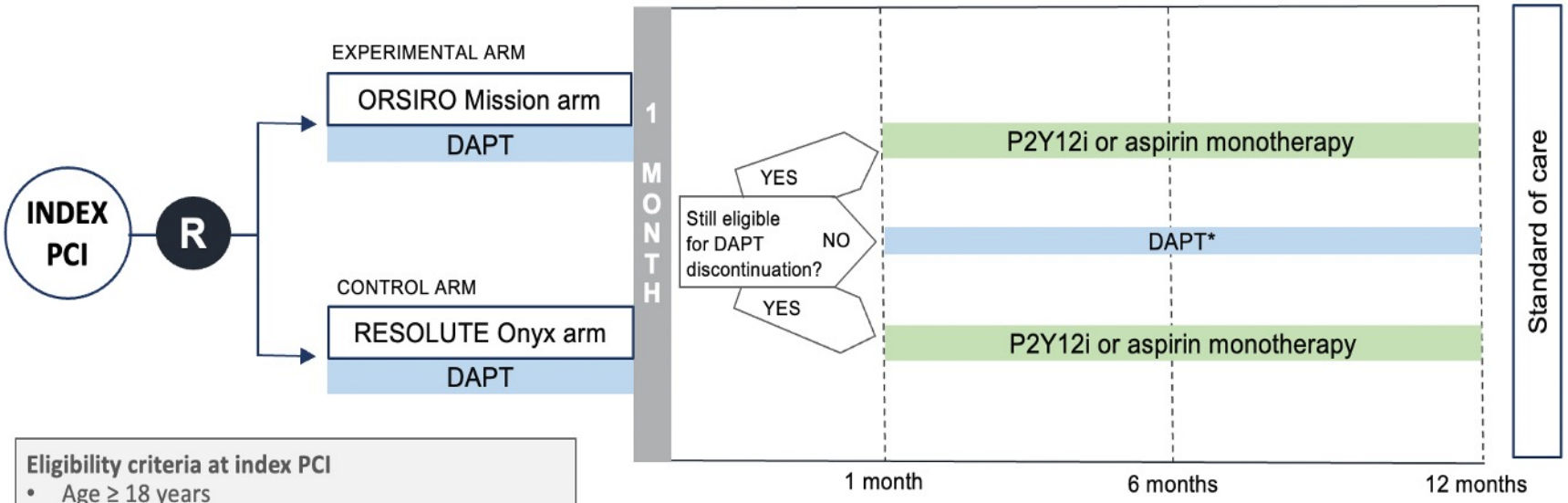
- Randomized and non-randomized studies have shown that 1-month DAPT after PCI reduces bleeding without compromising safety compared with more prolonged treatment durations in patients at high bleeding risk (HBR).[1,2]

- However, there is limited information on the comparative efficacy and safety of different stent platforms in HBR patients undergoing an abbreviated DAPT duration after PCI.

- Onyx ONE compared 2 drug-eluting stent platforms in patients at high bleeding risk undergoing 1 month of DAPT and showed that durable-polymer zotarolimus-coated stents were associated with non-inferior outcomes to polymer-free umirolimus-coated stents.[3]

1. Valgimigli M et al. N Engl J Med. 2021;385:1643-1655. 2. Mehran R et al. JACC Cardiovasc Interv. 2021;14:1870-1883.
3. Windecker S et al *N Engl J Med*. 2020;382:1208-1218

Study Design



Eligibility criteria at index PCI

- Age ≥ 18 years
- Acceptable candidate for treatment with DES
- Patient at HBR
- Able to comply with all protocol and follow-up requirements
- Eligible for 1-month DAPT

12-month primary endpoint
The composite of cardiac death, myocardial infarction and definite or probable ST

* Subjects will not be excluded from the study but will be assessed at each follow-up visit through 12 months.

High Bleeding Risk Definition (1 or more criteria)

a. ≥ 75 years of age

b. Moderate or severe chronic kidney disease or failure

c. Advanced liver disease

d. Cancer diagnosed or treated within the previous 12 months or actively treated

e. Anemia with hemoglobin < 11.0 g/dL or requiring transfusion within 4 weeks before randomization

f. Baseline thrombocytopenia

g. History of stroke, previous intracerebral hemorrhage (ICH) or presence of a brain arteriovenous malformation

h. History of hospitalization for bleeding within previous 12 months

i. Chronic clinically significant bleeding diathesis

j. Clinical indication for chronic or lifelong oral anticoagulation (OAC)

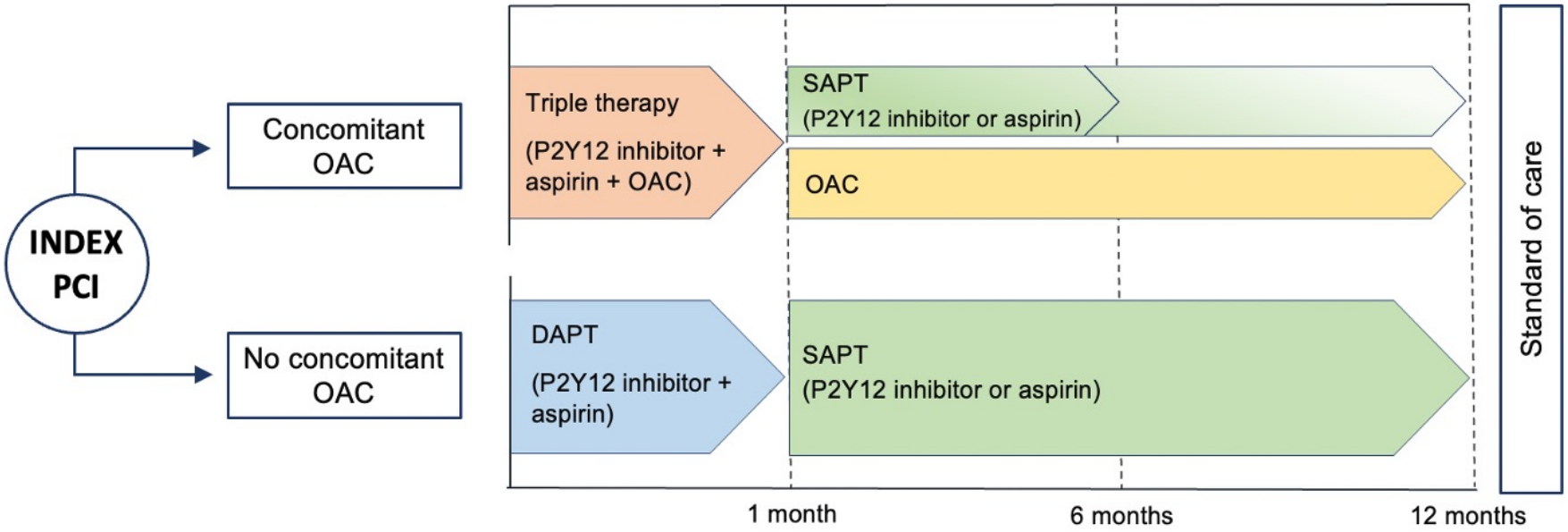
k. Clinical indication for chronic steroid or oral non-steroidal anti-inflammatory drug(s) other than aspirin

l. Non-deferrable major surgery on DAPT

m. Recent major surgery or major trauma within 30 days before PCI

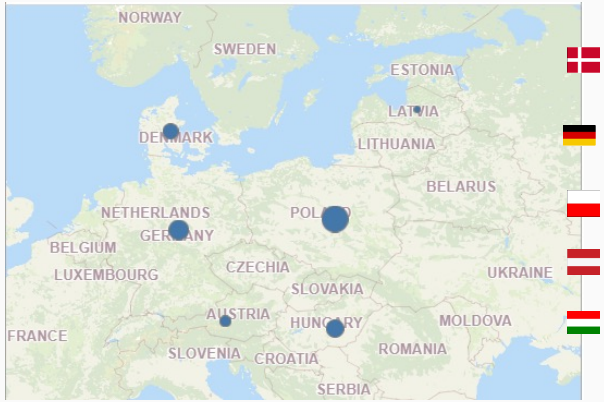
n. PRECISE DAPT score ≥ 25

Medication Chart



Landi A et al. 2023. J Cardiovasc Transl Res. doi: 10.1007/s12265-023-10400-x

52 Enrolling Sites in 18 Countries



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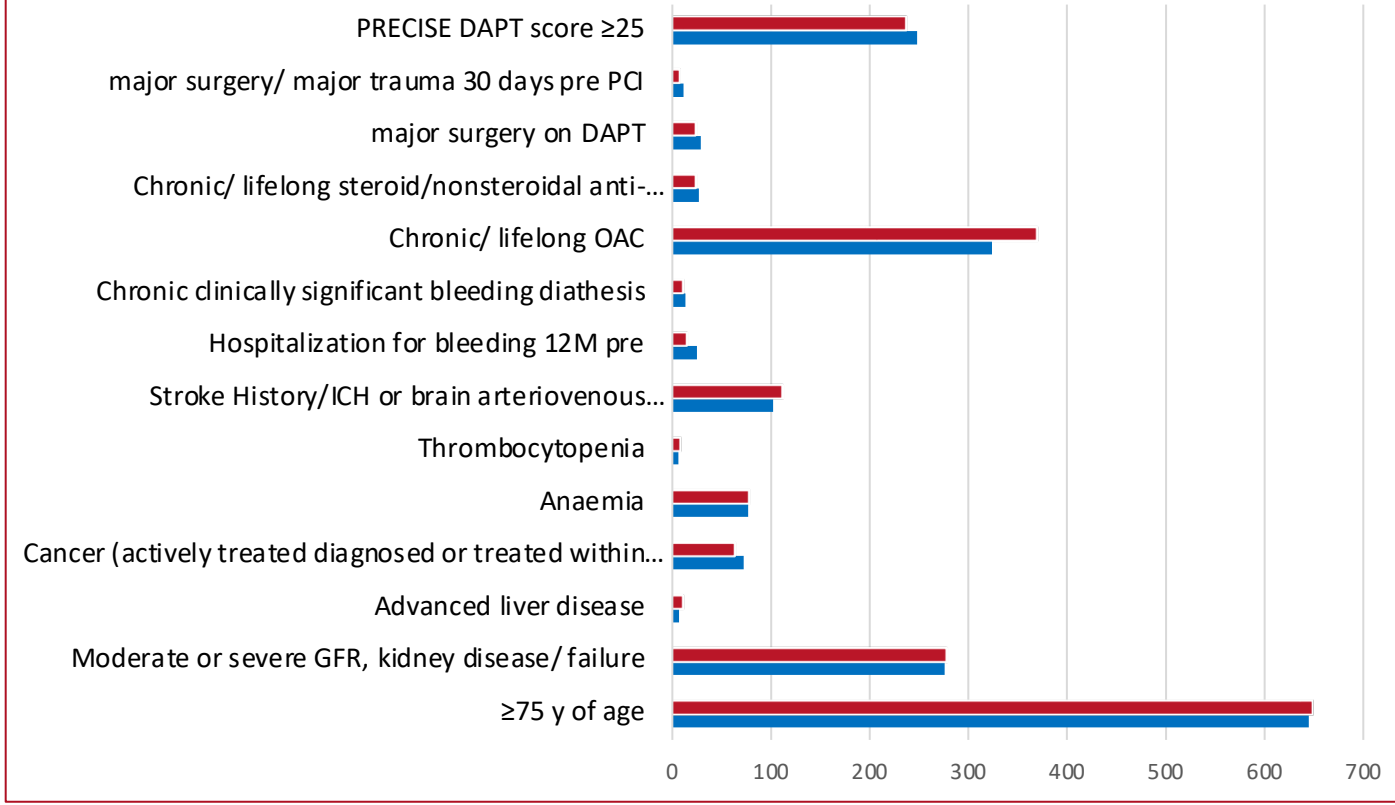
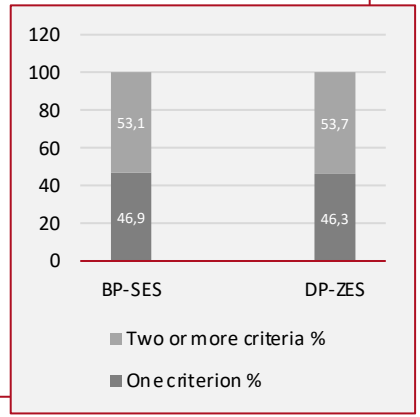
Patient Characteristics (N=1948 pts)

Characteristic	BP-SES (n=969 Patients)	DP-ZES (n=979 Patients)
Age [years] Mean ± SD	76.0 ± 8.5	75.6 ± 8.2
Male	658 (67.9)	679 (69.4)
Renal disease	321 (33.1)	323 (33.0)
Hepatic disease	30 (3.1)	32 (3.3)
Respiratory disease	142 (14.7)	136 (13.9)
Hypertension	787 (81.2)	804 (82.1)
Hypercholesterolemia	659 (68.0)	678 (69.3)
Diabetes	301 (31.1)	311 (31.8)
Smoking History		
Ex-smoker	317 (32.7)	324 (33.1)
Current smoker	131 (13.5)	120 (12.3)
Congestive heart failure	215 (22.2)	202 (20.6)
Oral anticoagulant	324 (33.4)	369 (37.8)
Stable angina	477 (49.6)	495 (50.9)
Silent ischemia	190 (19.8)	197 (20.3)
Non–ST-elevation myocardial infarction	182 (19.0)	180 (18.5)
ST-elevation myocardial infarction	16 (1.7)	17 (1.7)

High-Bleeding Risk Criteria





Procedural Characteristics at Patient Level (1)

Characteristic	Biodegradable-Polymer Stent (n=969 Patients)	Zotarolimus-Eluting Stent (n=979 Patients)
Access[b], no. (%)		
Radial	815 (84.1)	834 (85.2)
Femoral	137 (14.1)	130 (13.3)
Brachial	10 (1.0)	9 (0.9)
Lesion location[c], no. (%) (at least 1 lesion)		
Left main	45 (3.7)	38 (3.9)
Left anterior descending	529 (55.2)	541 (55.6)
Left circumflex	270 (28.2)	264 (27.1)
Right coronary artery	310 (32.3)	299 (30.7)
Bypass graft	16 (1.7)	15 (1.5)
At least one B2/C lesion class[c], no. (%)	583 (60.9)	614 (63.5)
At least one lesion with moderate or severe calcification‡, no. (%)	339 (35.3)	335 (34.5)
At least one lesion with bifurcation[c], no. (%)	290 (30.2)	308 (31.7)

a Plus–minus values are means±SD.

b Unknown for 7 patients in biodegradable-polymer stent group and 6 patients in the zotarolimus-eluting stent group.

c Unknown for 10 patients in biodegradable-polymer stent group and 6 patients in the zotarolimus-eluting stent group (percentages were calculated using a total of 959 patients in the biodegradable-polymer stent group and 973 patients in the zotarolimus-eluting stent group).

Procedural Characteristics at Patient Level (2)

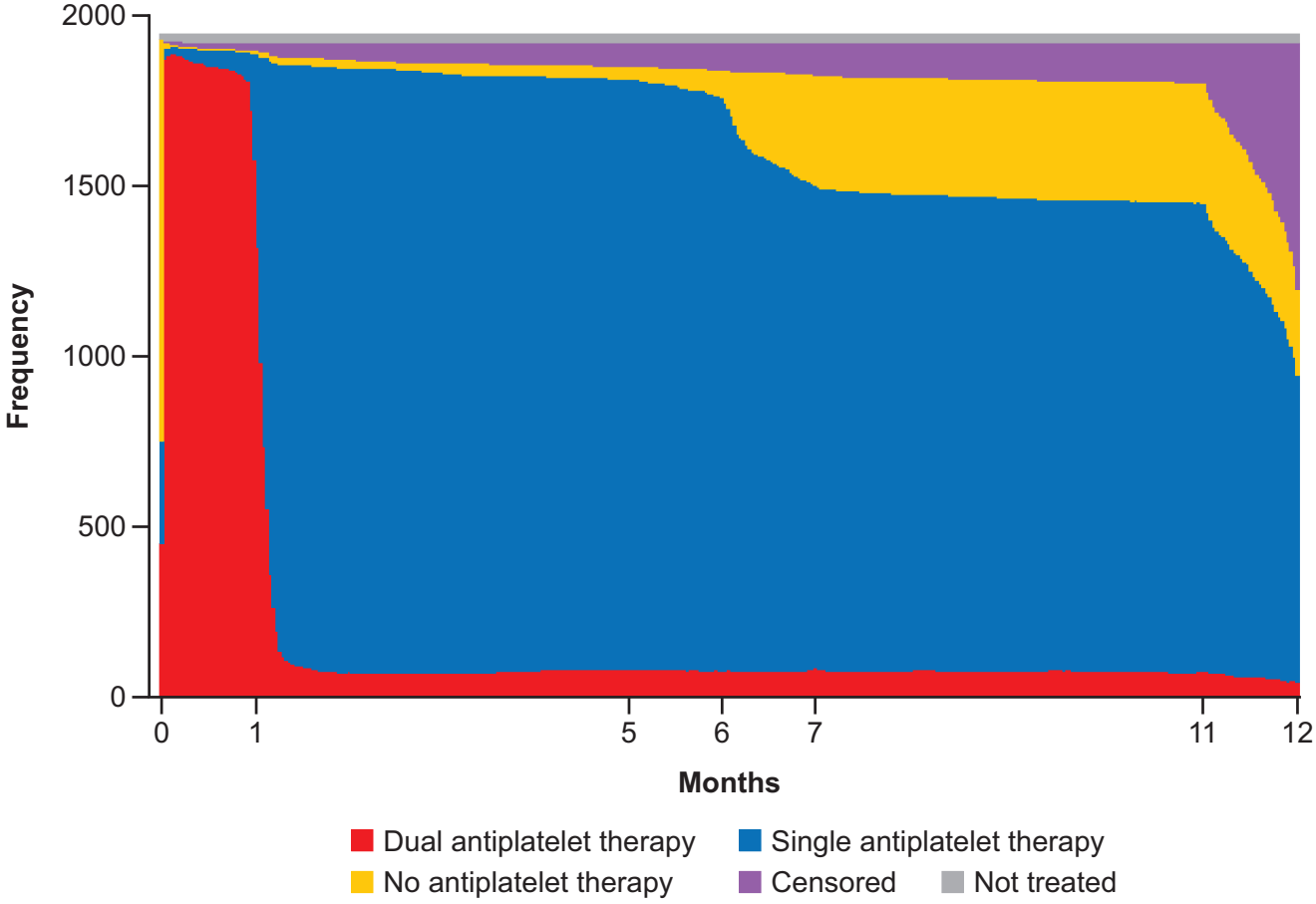
Characteristic	Biodegradable-Polymer Stent (n=969 Patients)	Zotarolimus-Eluting Stent (n=979 Patients)
≥ 1 lesion with chronic total occlusion[c], no. (%)	24 (2.5)	22 (2.3)
≥ 1 lesion with in-stent restenosis[c], no. (%)	47 (4.9)	50 (5.1)
Mean reference vessel diameter per subject[c], mm	3.1 ± 0.5	3.1 ± 0.5
Mean diameter stenosis per subject[c], %	82.0 ± 11.8	82.2 ± 13.0
Mean lesion length per subject[c], mm	20.8 ± 11.1	21.3 ± 12.2
Multivessel intervention, no. (%)	210 (21.9)	181 (18.6)
Number of vessels treated per patient[d], no. (%)		
One	738 (77.0)	779 (80.1)
Two	173 (18.0)	150 (15.4)
Three	33 (3.4)	24 (2.5)
Number of stents per patient	1.7 ± 1.0	1.7 ± 1.0
Total stent length per patient	37.2 ± 25.4	36.7 ± 24.4
Any overlapping stenting, no. (%)	174 (18.0)	212 (21.7)

a Plus–minus values are means±SD.

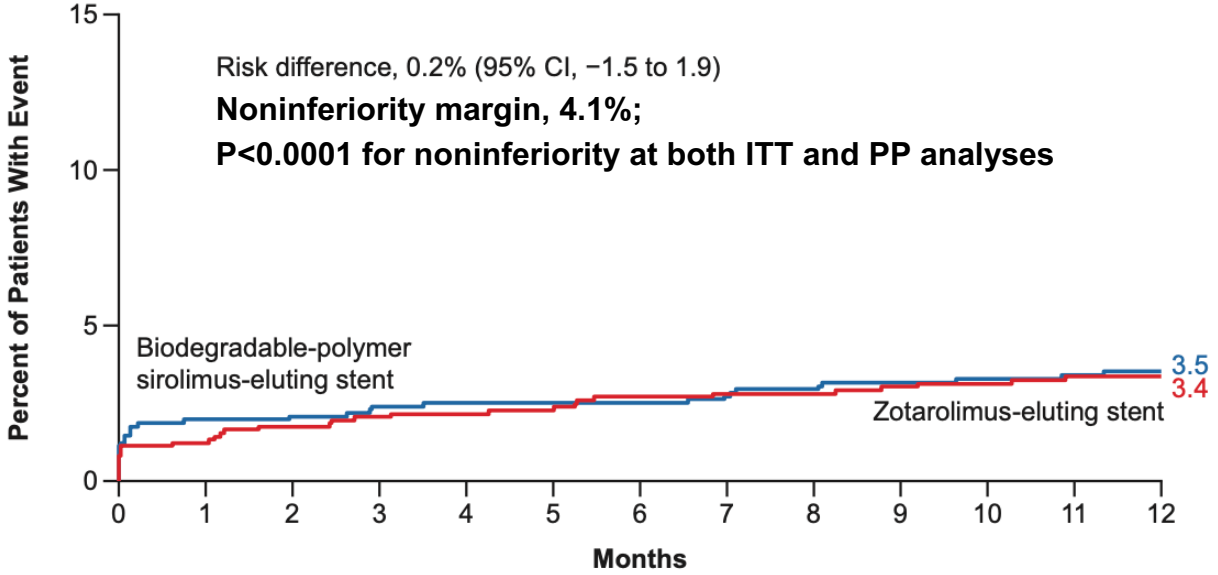
c Unknown for 10 patients in biodegradable-polymer stent group and 6 patients in the zotarolimus-eluting stent group (percentages were calculated using a total of 959 patients in the biodegradable-polymer stent group and 973 patients in the zotarolimus-eluting stent group).

d Four patients in the biodegradable-polymer stent group and 6 in the zotarolimus-eluting stent group had 4 treated vessels; 1 patient in the zotarolimus-eluting stent group had 5 treated vessels and 11 patient in biodegradable-polymer stent group and 13 in the zotarolimus-eluting stent group had only coronary artery bypass graft treatment.

Adherence to Antiplatelet Therapy after PCI



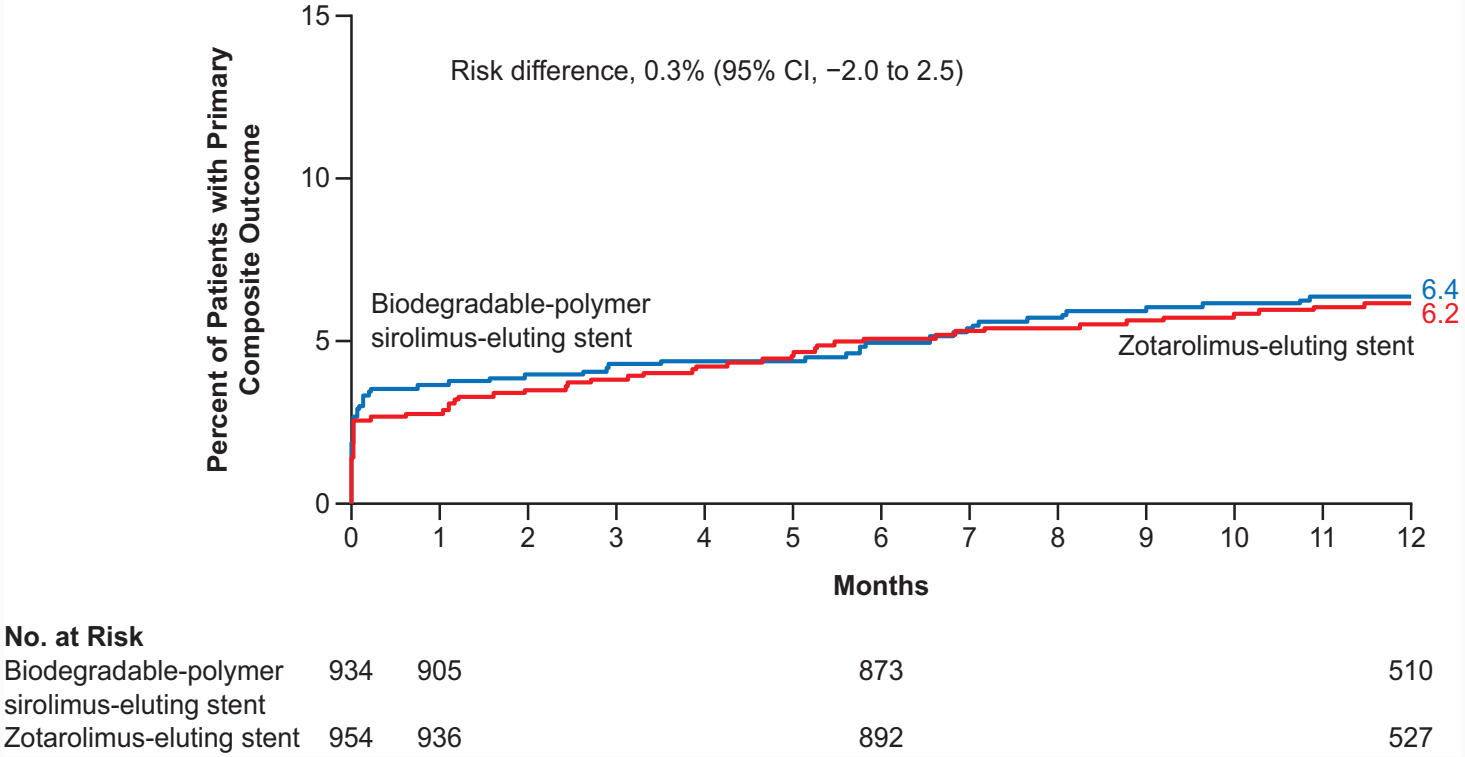
Primary Outcome: Cardiac Death, Myocardial Infarction*, or Stent Thrombosis



No. at Risk				
Biodegradable-polymer sirolimus-eluting stent	941	921	896	526
Zotarolimus-eluting stent	960	950	913	537

*ARC-2 definition

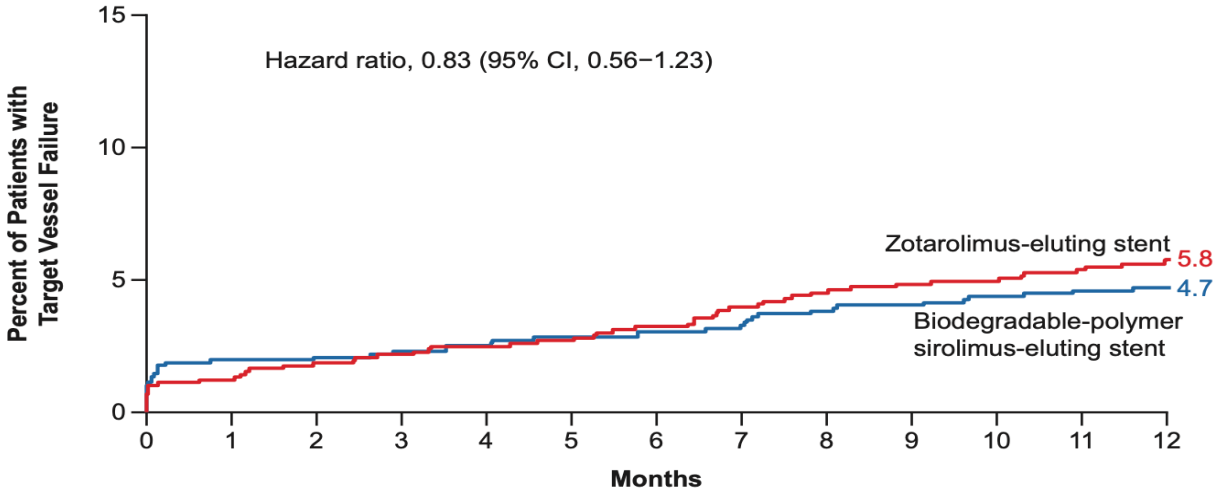
Prespecified EP: Cardiac Death, Myocardial Infarction*, or Stent Thrombosis



No. at Risk				
Biodegradable-polymer sirolimus-eluting stent	934	905	873	510
Zotarolimus-eluting stent	954	936	892	527

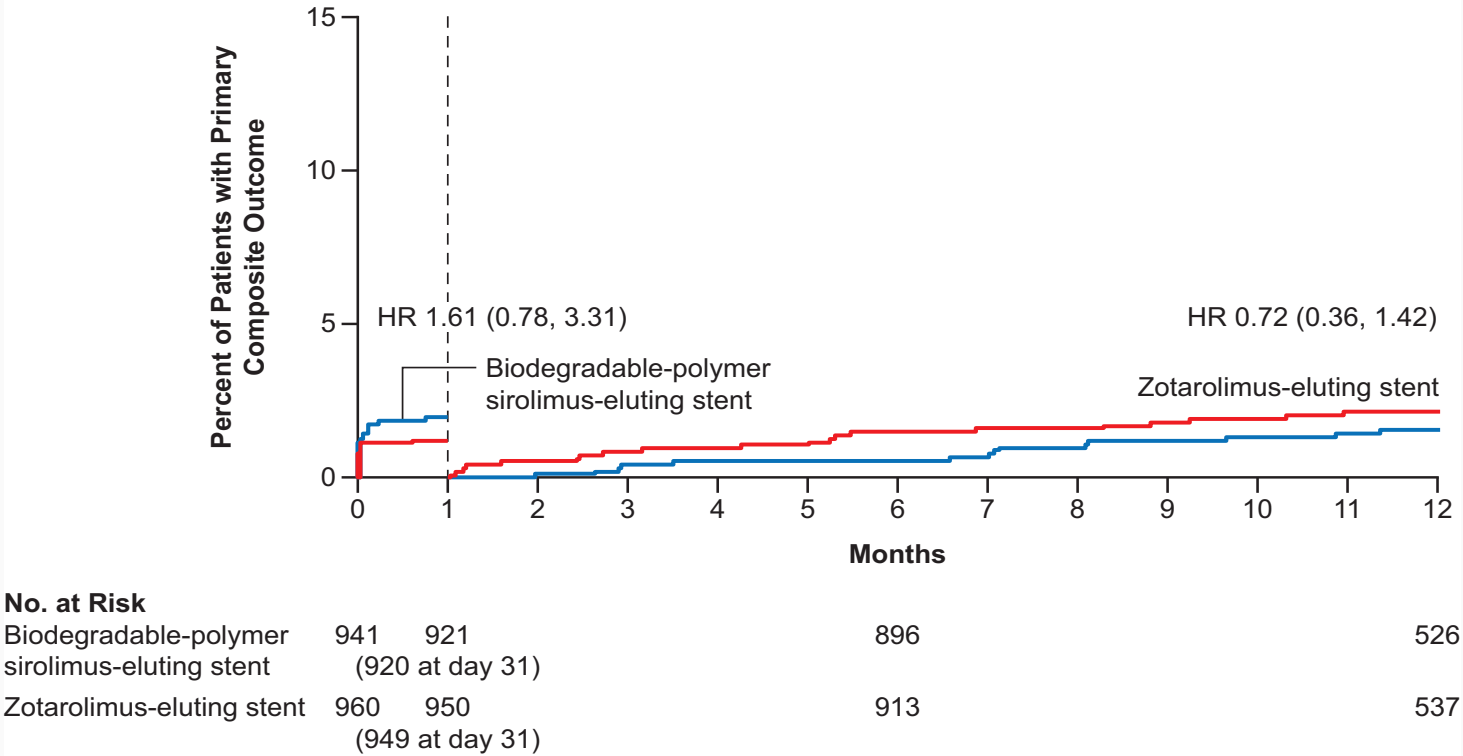
*Third Universal MI definition

Target Vessel Revascularization



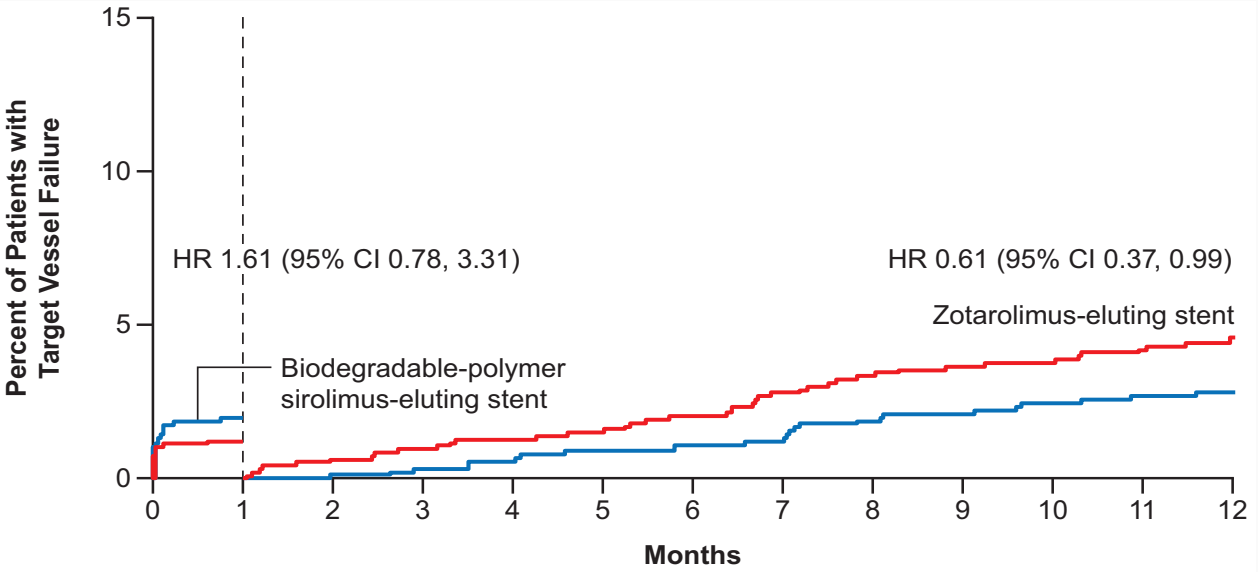
No. at Risk				
Biodegradable-polymer sirolimus-eluting stent	942	921	891	518
Zotarolimus-eluting stent	961	950	909	527

Prespecified Landmark Analysis at 30 days: Primary Endpoint*



*: ARC-2 definition

Prespecified Landmark Analysis at 30 days: Target Vessel Failure



No. at Risk

Biodegradable-polymer sirolimus-eluting stent	942	921 (920 at day 31)	891	518
Zotarolimus-eluting stent	961	950 (949 at day 31)	909	527

Limitations

- Incidences of outcome events at 1 year were lower than expected
- Treatments were open label
- Decision to continue aspirin or a $P2Y_{12}$ inhibitor was at the discretion of the physicians (Rx was stratified accordingly)
- Complete SDV was implemented in a random cohort of 28.2% of the patients
- Angiograms were not assessed by an independent core-laboratory

Conclusion

In patients at high risk for bleeding, a strategy of PCI with BP-SES (Orsiro) followed by 30 days of DAPT therapy was non-inferior to DP-ZES (Onyx) with respect to the incidence of death from cardiac causes, myocardial infarction, or stent thrombosis

Circulation

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BIODEGRADABLE-POLYMER OR DURABLE-POLYMER STENTS IN PATIENTS AT HIGH BLEEDING RISK. A RANDOMIZED, OPEN-LABEL CLINICAL TRIAL

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