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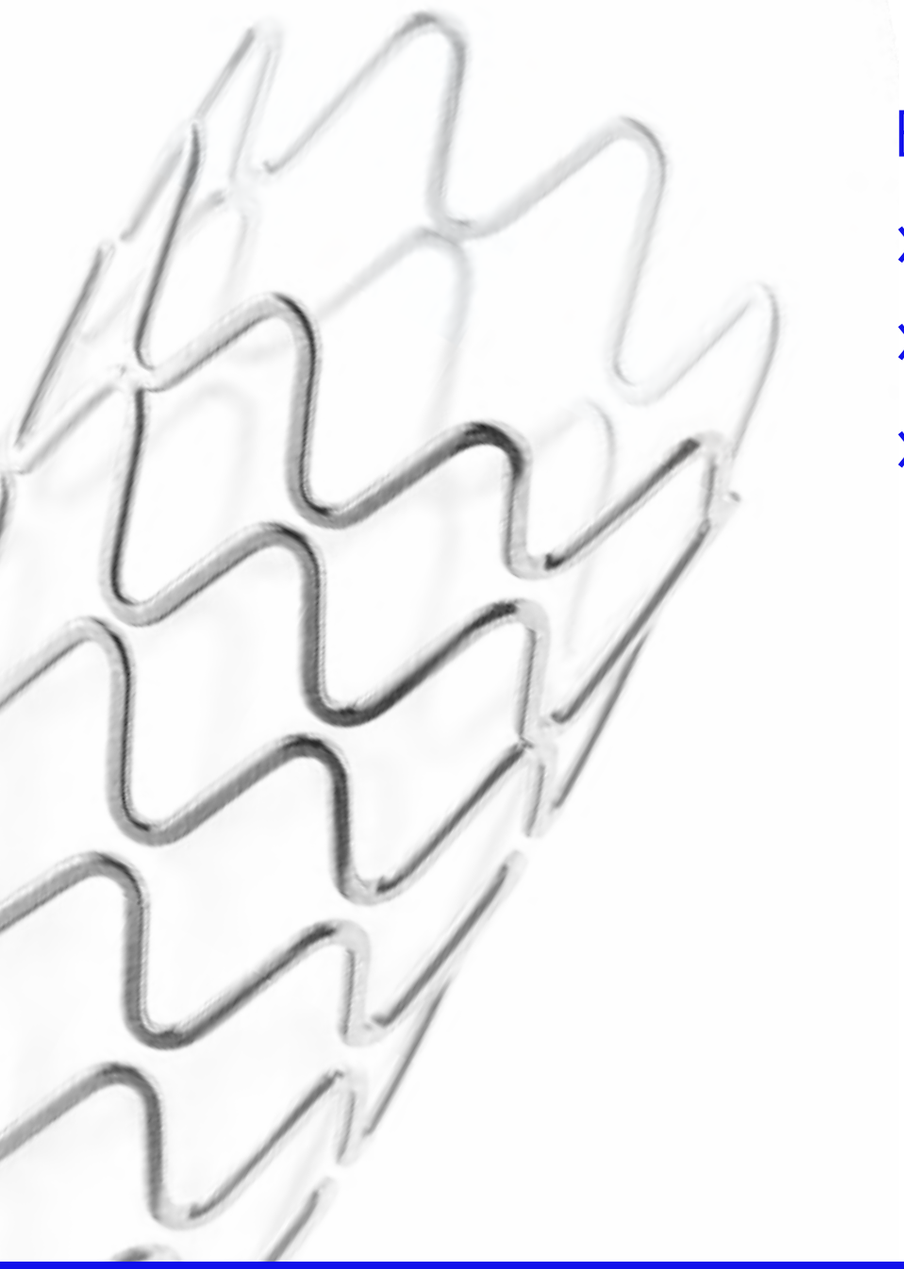
Onyx ONE clinical summary



Background

- Onyx ONE overview
- Short-DAPT trials comparison
- Why Resolute Onyx™ DES for HBR patients on 1-month DAPT?

Clinical data

- Onyx ONE global trial 1-year results
- Onyx ONE global trial 2-year results
- Onyx ONE Clear analysis 1-year results
- Onyx ONE Clear analysis 2-year results
- ACS subanalysis
- AF subanalysis
- Complex PCI subanalysis
- Sex subanalysis
- Diabetic subanalysis
- Bifurcation subanalysis

Onyx ONE overview

Onyx ONE global trial

First, randomised, 1-month DAPT trial comparing a DES to a DES in high bleeding risk (HBR) patients and proving Resolute Onyx™ DES safety and efficacy.[1]

First DES CE indicated for 1-mo DAPT in HBR patients

ACS subgroup[3]
ESC 2020

Real-world, HBR patient population led to **meaningful subanalyses** for greater confidence making short-DAPT decisions

Onyx ONE Clear analysis

Evaluated Resolute Onyx DES in ~1500 complex HBR patients on 1-month DAPT and reinforced safety and efficacy results from the Onyx ONE global trial.[2]

First DES FDA approved for HBR patients with 1-mo DAPT

AF subgroup[4]
TCT 2020

Complex PCI subgroup[5]
TCT 2020

Sex subgroup[6]
SCAI 2021

Diabetic subgroup[7]
PCR 2021

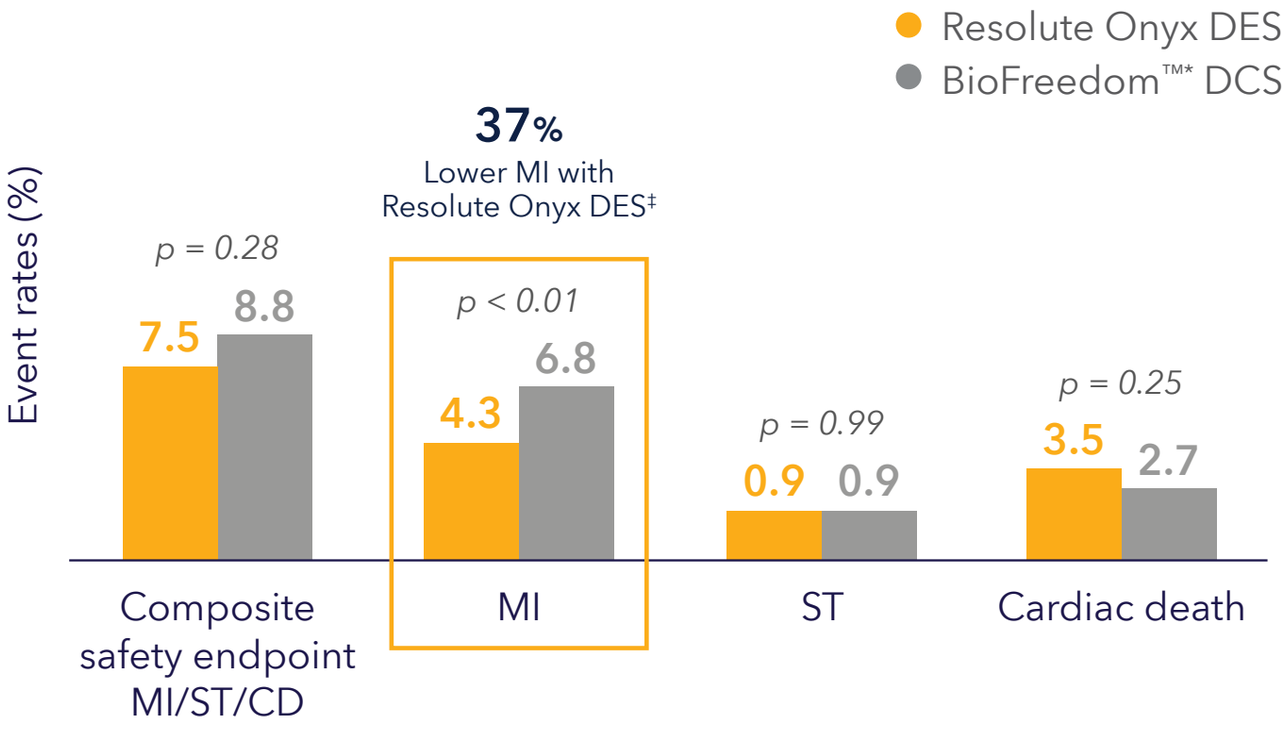
Bifurcation subgroup[8]
TCT 2021

[1]Windecker S, et al. *N Engl J Med*. 2020;382:1208-1218.
[2]Kandzari D, et al. *Circ Cardiovasc Interv.* 2020;13: e009565.
[3]Kedhi A, et al. Outcomes in HBR with ACS with 1-Month DAPT. Presented at ESC 2020.
[4]Pasupati S, et al. Ischemic and Bleeding Outcomes in Patients With vs. Without AF. Presented at TCT 2020.
[5]Kandzari D, et al. Complex PCI with 1-month DAPT in HBR Patients. Presented at TCT 2020.
[6]Mehran, R et al. Sex-based Outcomes after PCI in Complex High Bleeding Risk Patients: Results from the Onyx ONE Clear Trial. Presented at SCAI 2021.
[7]Kedhi E, et al. Diabetic High Bleeding Risk Patients with One-Month DAPT: Onyx ONE Clear Results. Presented at Euro PCR 2021.
[8]Kirtane A, et al. Clinical Outcomes in High Bleeding Risk Patients with Bifurcations after PCI with Resolute Onyx DES and One Month Dual Antiplatelet Therapy. Presented at TCT 2021.

Onyx ONE global trial 1-year results

Showed Resolute Onyx™ DES was safe and effective in HBR patients on 1-month DAPT

Landmark analysis after DAPT discontinuation† showed low event rates



*Third-party brands are trademarks of their respective owners.
†From 1 month to 1 year. Rates are taken from Kaplan-Meier estimates.
‡Post-hoc analyses were not powered.
Source: Windecker S, et al. *N Engl J Med.* 2020;382:1208-1218.

Read the Onyx ONE global trial article printed in *The New England Journal of Medicine*

- Randomised controlled trial
- Compared Resolute Onyx DES to BioFreedom DCS in ~2000 HBR patients on 1-month DAPT
- 1.6 high bleeding risk criteria per patient
- BARC 3–5 bleeding rate:
  - Resolute Onyx 4.9%
  - BioFreedom DCS 4.4% p = 0.67
- Primary endpoint met with Resolute Onyx DES (17.1%) noninferior to BioFreedom DCS (16.9%) for cardiac death (CD), myocardial infarction (MI), and stent thrombosis (ST)
- Resolute Onyx was the first DES CE indicated for 1-month DAPT in HBR patients based on the results from this study

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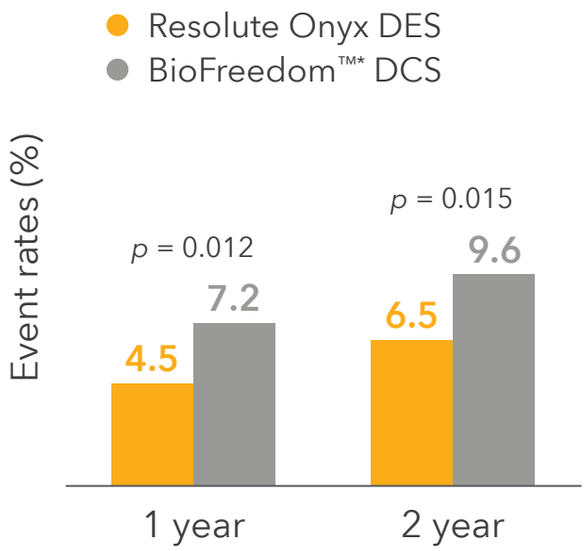
Onyx ONE global trial
2-year results

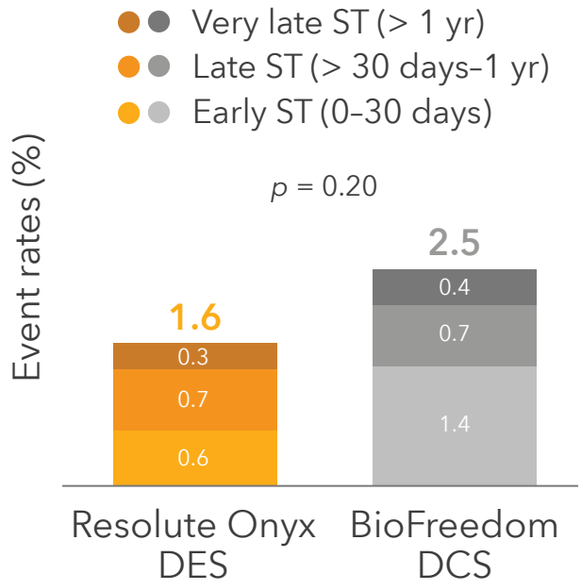
Reinforced Resolute Onyx™ DES safety and efficacy in HBR patients on 1-month DAPT at two years

- Final follow-up of the Onyx ONE global trial at two years
- 1.6 high bleeding risk criteria per patient
- No difference between Resolute Onyx DES (21.3%) and BioFreedom DCS (20.7%) for cardiac death (CD), myocardial infarction (MI), and stent thrombosis (ST)
- Significantly lower cd-TVR† with Resolute Onyx DES (4.8%) compared to BioFreedom DCS (7.1%) (p = 0.035)

Significantly lower spontaneous MI with Resolute Onyx DES†



Low stent thrombosis confirmed at 2-year follow-up†



*Third-party brands are trademarks of their respective owners.
†Endpoints were not powered.
Source: Windecker S, et al. Final Two-Year Results from the Randomized Onyx ONE Trial in High Bleeding Risk Patients Treated with 1-month DAPT. Presented at ACC 2021.

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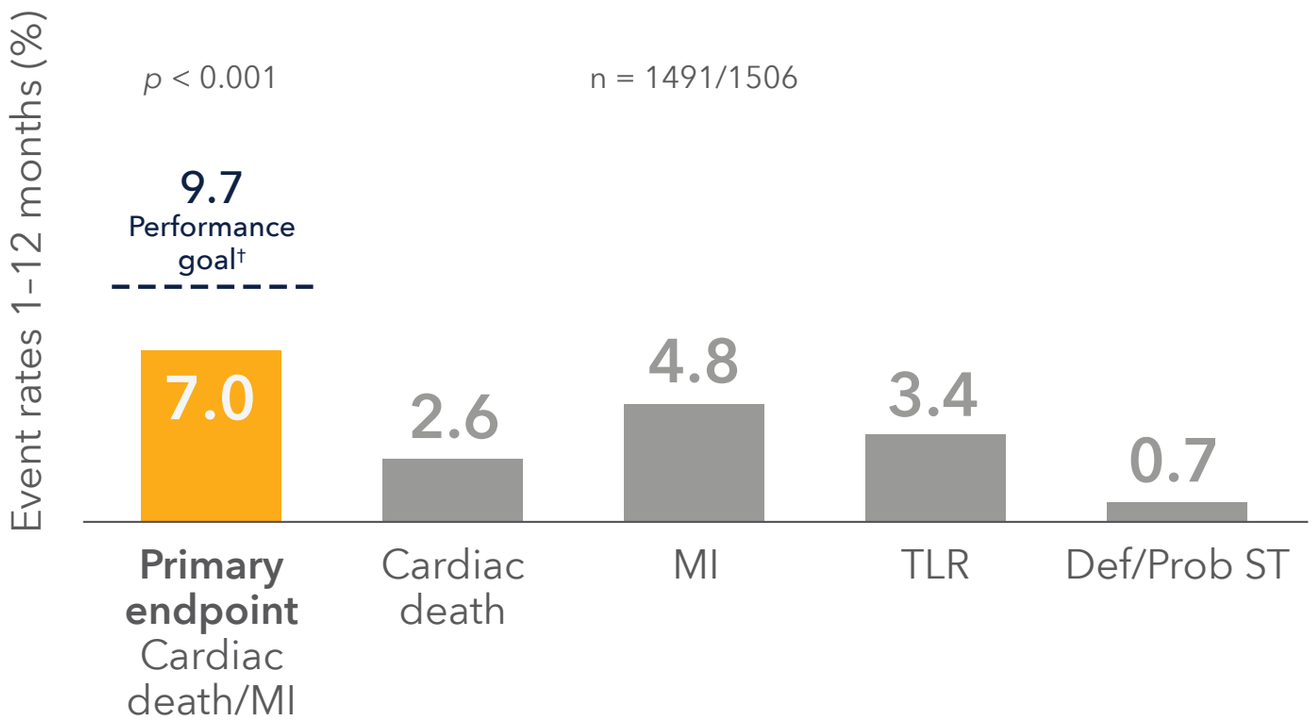
Onyx ONE Clear analysis

Reinforced Resolute Onyx™ DES was safe and effective in HBR patients on 1-month DAPT

Beat performance goal derived from contemporary 1-month DAPT trials†



†ZEUS, LEADERS FREE, and SENIOR trials.
Source: Kandzari DE, et al. *Circ Cardiovasc Interv*. 2020;13:e009565.

Read the Onyx ONE Clear analysis article printed in *Circulation: Cardiovascular Interventions*

- Prospective, multicentre, single-arm analysis
- ~1500 patients included in primary endpoint analysis
- 1.6 high bleeding risk criteria per patient
- 4% BARC 3–5 bleeding rate at 1 year
- Primary endpoint results showed 7.0% cardiac death or myocardial infarction at 1 year, beating the performance goal of 9.7%
- Resolute Onyx was the first DES FDA indicated for HBR patients with 1-month DAPT labeling based on the results from this analysis

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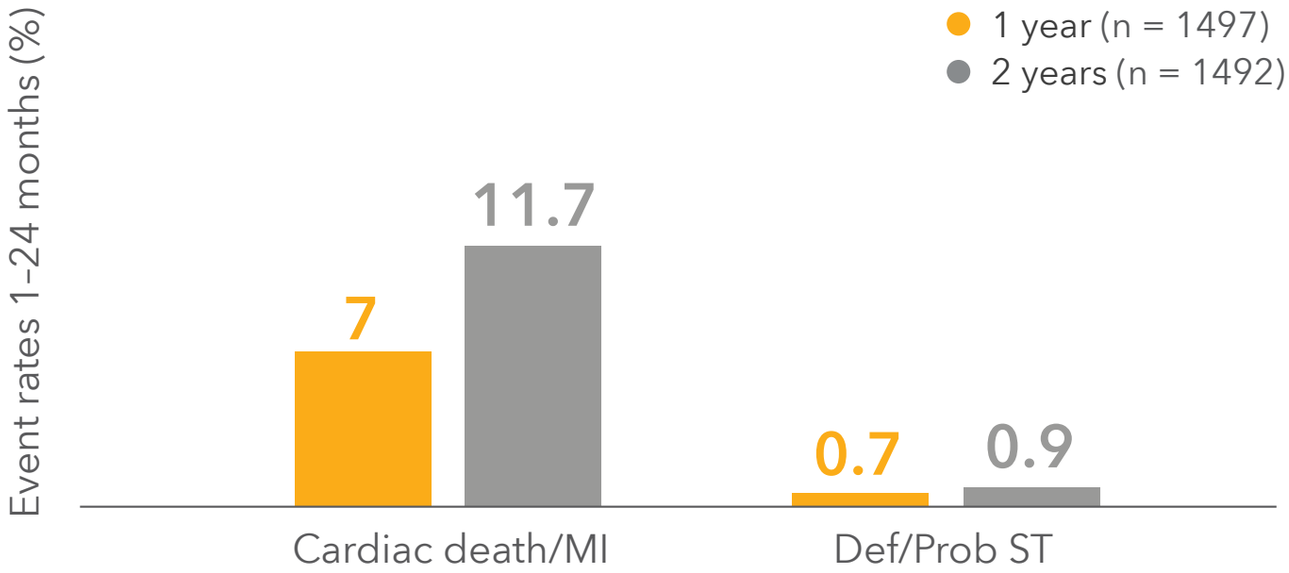
Onyx ONE Clear analysis 2-year results

Low cardiac death/MI and stent thrombosis confirmed at 2-year follow-up



Source: Kandzari D, et al. One-month Dual Antiplatelet Therapy after PCI with Resolute Onyx DES: Final 2-year Results from Onyx ONE Clear. Presented at TCT 2021.

Reinforced Resolute Onyx DES safety and efficacy in HBR patients on 1-month DAPT at two years

- Final follow-up of the Onyx ONE Clear analysis at two years
- 1.6 high bleeding risk criteria per patient and 44.6% met ≥ 2 HBR criteria
- Low 0.9% ST rate at 2 years in highly complex HBR patient population treated with 1-month DAPT

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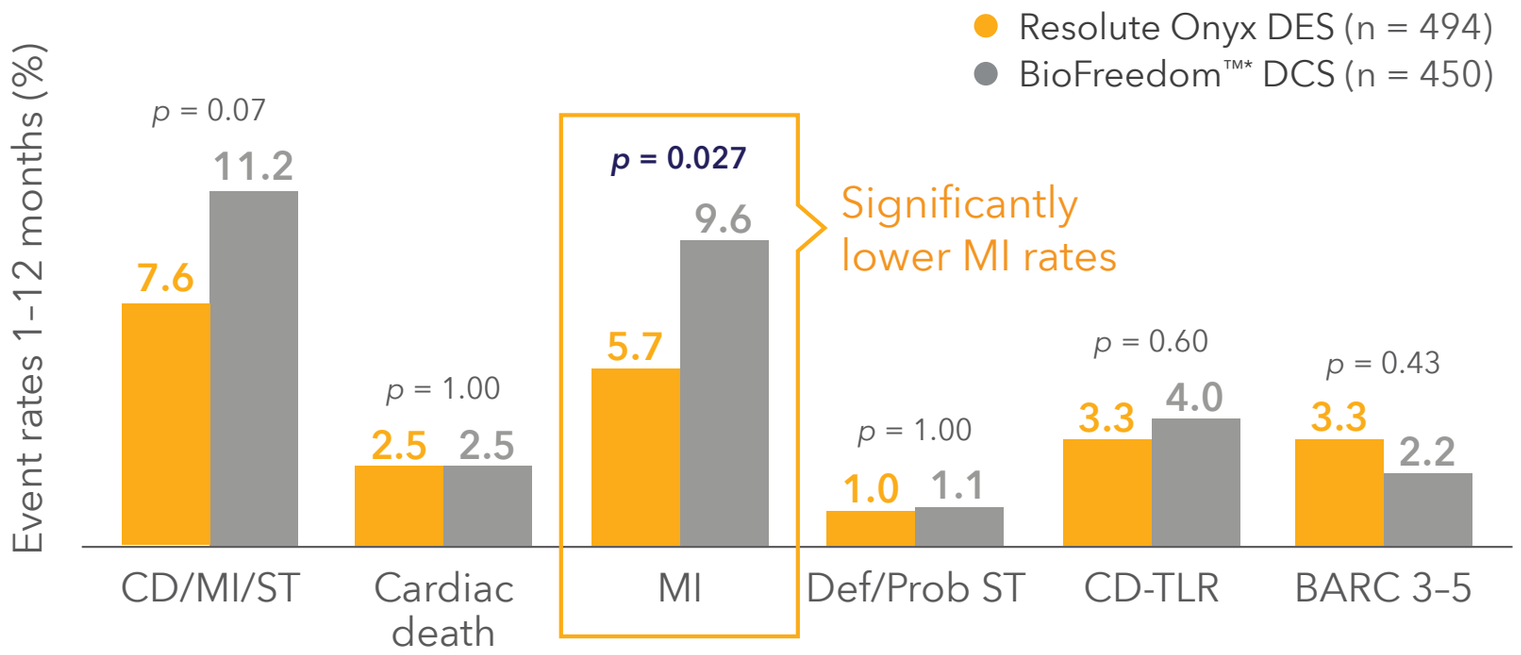
Acute coronary syndrome (ACS) subanalysis results

Resolute Onyx™ DES was safe and effective in HBR, ACS patients on 1-month DAPT†

Significantly lower MI in high ischemic risk patients‡



- Prespecified subanalysis from Onyx ONE global trial
- Compared Resolute Onyx DES to BioFreedom DCS
- 53% HBR ACS patients (n = 944)
- 1.7 average high bleeding risk criteria per patient
- Significantly higher device success with Resolute Onyx DES (92%) vs. BioFreedom DCS (87%) p = 0.001

*Third-party brands are trademarks of their respective owners.
†Results not adjusted for multiple comparisons.
‡Endpoints were not powered.
Source: Kedhi A, et al. Outcomes in High Bleeding Risk Patients with Acute Coronary Syndrome with 1-Month DAPT: Insights from the Onyx ONE Trial. Presented at ESC Congress 2020.

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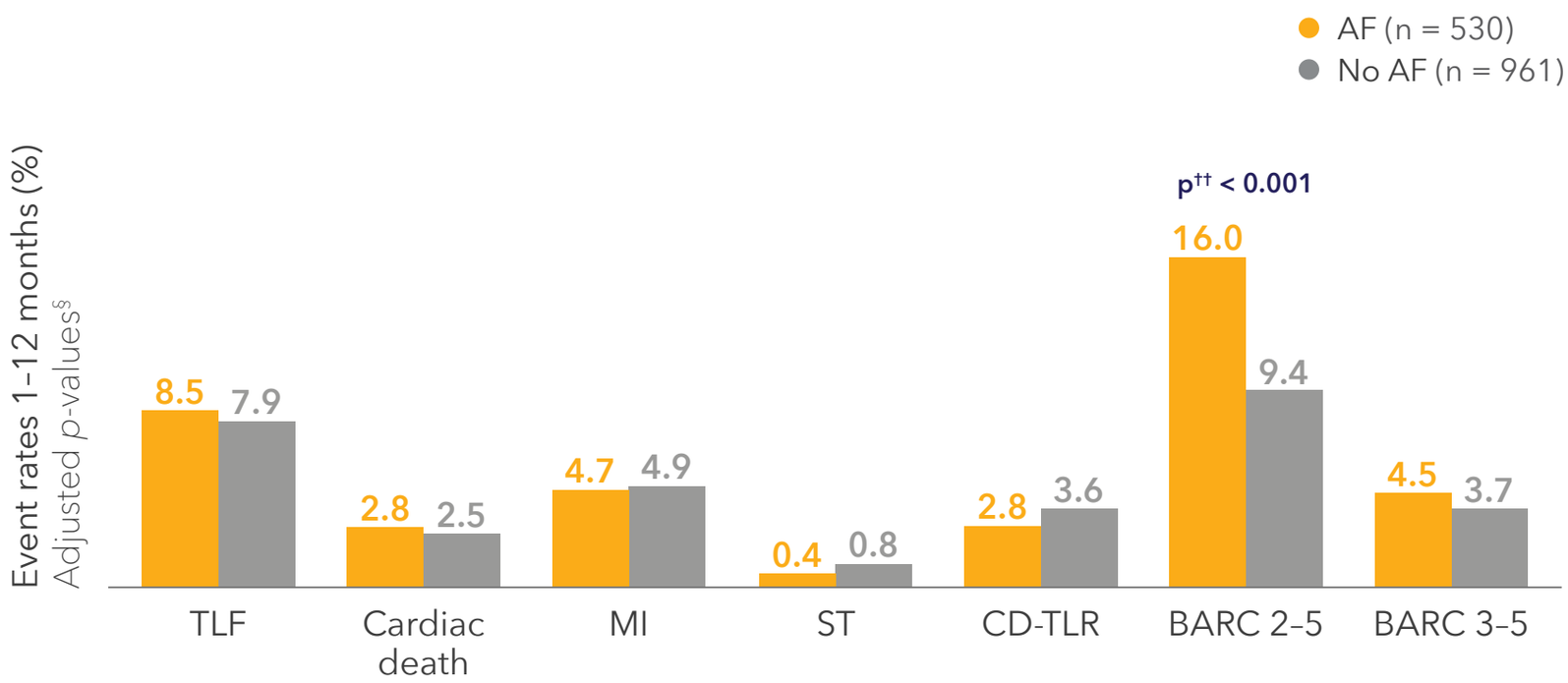
Atrial fibrillation (AF) subanalysis

Resolute Onyx™ DES was safe and effective in HBR, AF patients on 1-month DAPT†

No difference in ischemic events and bleeding (BARC 3-5)‡



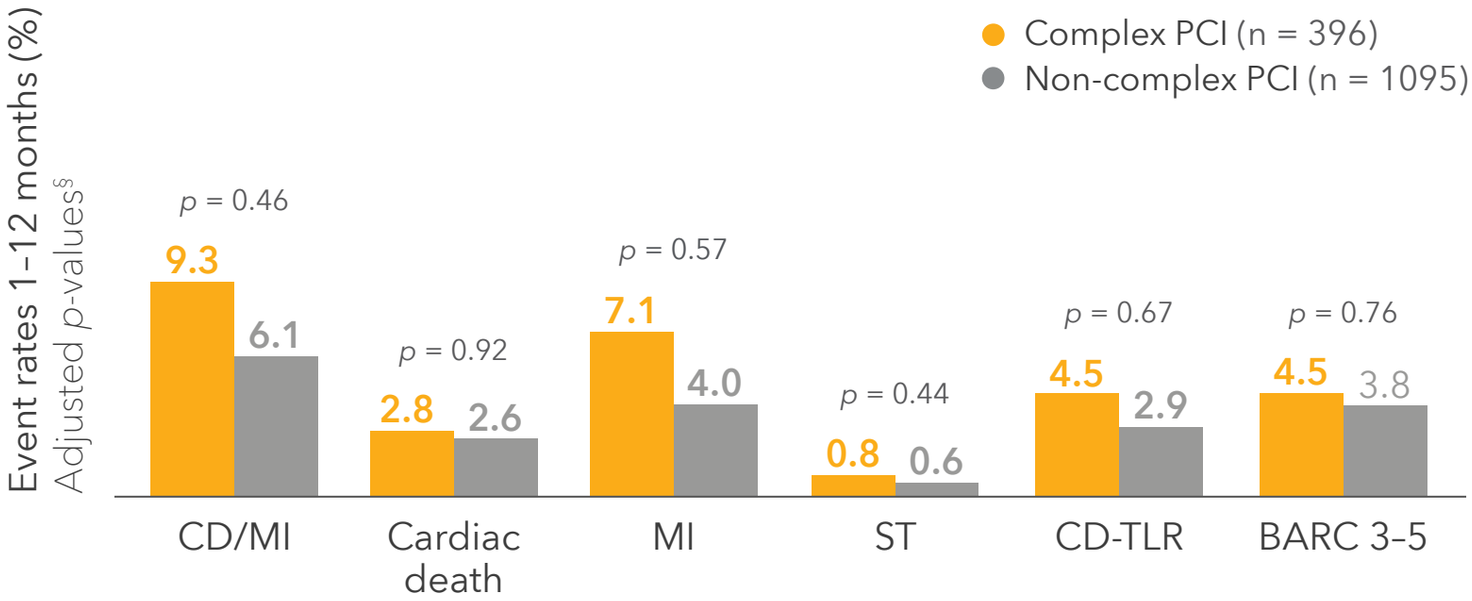
- Subanalysis from Onyx ONE Clear analysis
- AF patients are often on oral anticoagulants (OACs). Therefore, bleeding risk in patients on triple therapy (DAPT and OACs) is magnified.
- 36% HBR AF patients (n = 1491)
- Significantly higher average high bleeding risk criteria per AF patient (1.7) vs. no-AF patient (1.5, p < 0.001) with 87% of AF patients on oral anticoagulants

†Based on post-hoc analysis. Results not adjusted for multiple comparisons.
‡Endpoints were not powered.
§Propensity score method used to adjust for differences in baseline characteristics, all other P-values are not significant.
Source: Pasupati S, et al. Ischemic and Bleeding Outcomes in Patients With vs. Without Atrial Fibrillation: Analysis From the Onyx ONE Program. Presented at TCT Congress 2020.

Complex PCI subanalysis

Resolute Onyx™ DES was safe and effective in HBR, complex PCI patients on 1-month DAPT†

No difference in safety and efficacy despite increased lesion complexity‡



- Subanalysis from Onyx ONE Clear analysis
- Complex PCI patients met at least one characteristic[1]:
  - 3 vessels treated
  - ≥ 3 lesions treated
  - Total stent length > 60 mm
  - Bifurcation with ≥ 2 stents implanted
  - Use of any atherectomy device
  - Left main surgical bypass graft[Ω]
  - Chronic total occlusion
- 1.4 high bleeding risk criteria per patient in the complex PCI group
- Complex PCI group included significantly higher multivessel disease (78.3% vs. 39.5% p < 0.001) and B2/C lesions (84.2% vs. 75.5% p < 0.001)

†Based on post-hoc analysis. Results not adjusted for multiple comparisons.
‡Endpoints were not powered.
§Propensity score method used to adjust for differences in baseline characteristics.
ΩThe safety and effectiveness for stenting of saphenous vein grafts with the Resolute Onyx™ stent has not been established.
Source: Kandzari D, et al. Complex PCI with 1-month DAPT in High Bleeding Risk Patients: Analysis from the Onyx ONE Clear Study. Presented at TCT 2020.
[1] Dangas G, et al. *J Am Coll Cardiol.* 2020;75:2414-2424.

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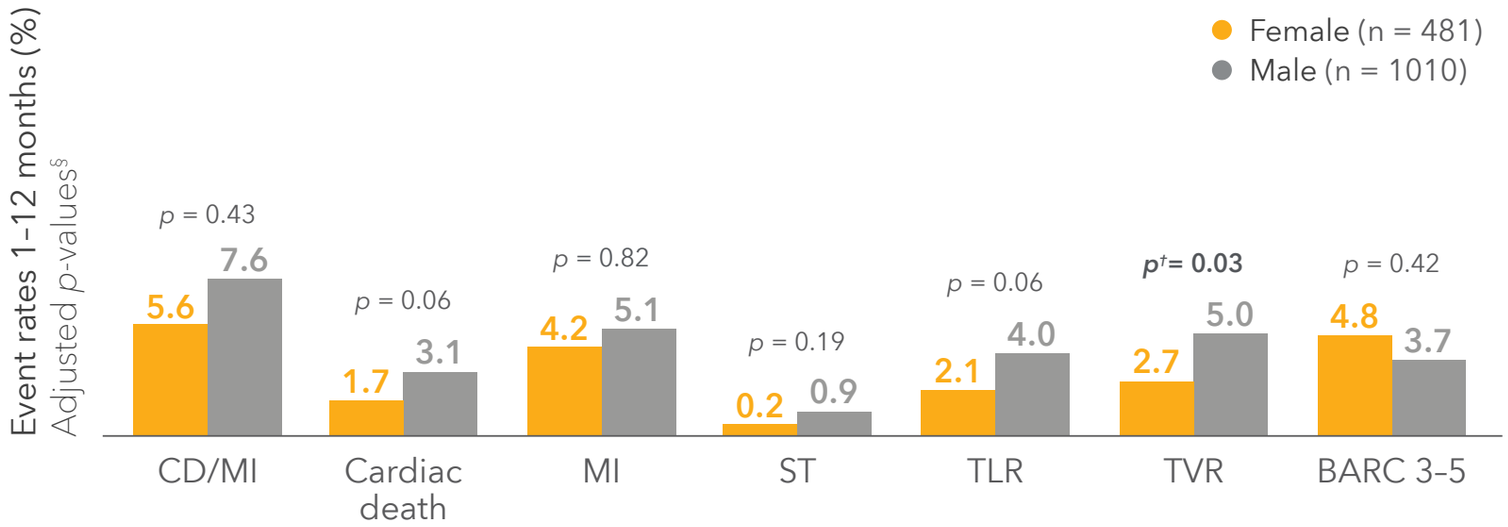
Sex subanalysis

Resolute Onyx™ DES was safe and effective in HBR, female or male patients on 1-month DAPT†

Low event rates including CD/MI and ST with no sex-based differences other than TVR‡



- Prespecified subanalysis from Onyx ONE Clear analysis
- 32% female population
- Significantly higher bleeding risk for females (1.6 average) vs. males (1.5 average) p = 0.02
- Differences in patient history and CAD symptoms highlight the need for sex-based analyses: ~28% non-STEMI in female patients but significantly higher prior interventions in men (previous PCI, CABG)

†Results not adjusted for multiple comparisons.
‡Endpoints were not powered.
§Propensity score method used to adjust for differences in baseline characteristics.
Source: Mehran, R et al. Sex-based Outcomes after PCI in Complex High Bleeding Risk Patients: Results from the Onyx ONE Clear Trial. Presented at SCAI 2021.

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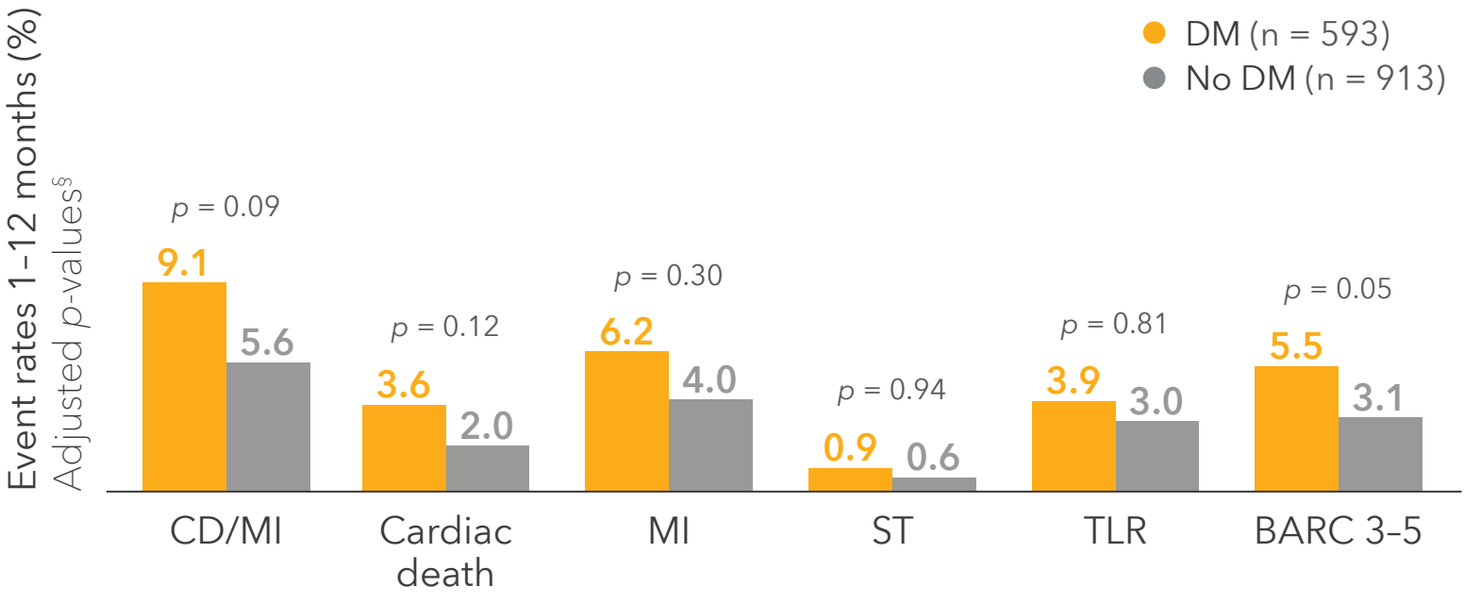
Diabetic subanalysis

No difference in safety and efficacy observed in DM vs. no-DM groups despite increased lesion complexity‡



Resolute Onyx™ DES was safe and effective in HBR patients with diabetes on 1-month DAPT†

- Prespecified subanalysis from Onyx ONE Clear analysis
- Patients with diabetes mellitus (DM) historically show a high risk for ischemic events
- 40% DM patients
- No difference in average high bleeding risk criteria per patient between DM (1.6) and no-DM (1.5, p = 0.06)
- DM patients experience higher comorbidities prior to interventions, and longer stent lengths

†Results not adjusted for multiple comparisons.
‡Endpoints were not powered.
§Propensity score method used to adjust for differences in baseline characteristics.
Source: Kedhi E, et al. Diabetic High Bleeding Risk Patients with One-Month DAPT: Onyx ONE Clear Results. Presented at Euro PCR 2021.

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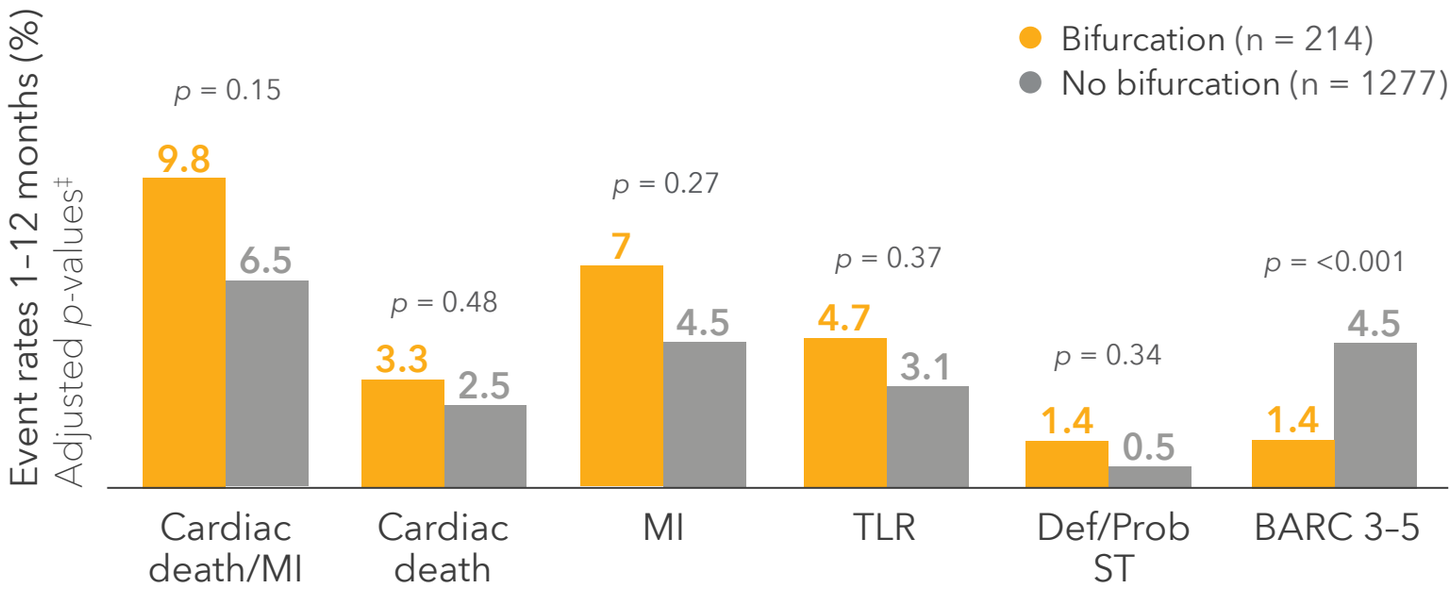
Bifurcation subanalysis

No difference in safety and efficacy in patients with bifurcation lesions despite increased complexity†



†Endpoints were not powered.
‡Results not adjusted for multiple comparisons. Propensity score method used to adjust for differences in baseline characteristics.
Source: Kirtane A, et al. Clinical Outcomes in High Bleeding Risk Patients with Bifurcations after PCI with Resolute Onyx DES and One Month Dual Antiplatelet Therapy. Presented at TCT 2021.

Resolute Onyx DES was safe and effective in HBR patients with bifurcation lesions on 1-month DAPT

- Prespecified subanalysis from the Onyx ONE Clear analysis
- 1.6 high bleeding risk criteria per patient
- Patients with bifurcation lesions had increased lesion complexity, procedure time, and total stented length
- Among 249 bifurcation lesions, 86% were treated with a provisional strategy and 14% with a planned two-stent strategy

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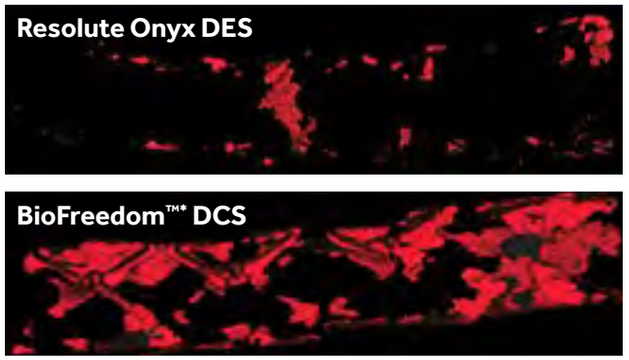
Short-DAPT trials comparison

	TRIAL DESIGN				LESION CHARACTERISTICS			PATIENT COMPLEXITY	
Name	Size	Comparator	Randomised control trial	Angiographic exclusions	B2/C	Average stented length	Moderate/ severe calcified lesions	ACS	Prior MI
Onyx ONE global trial[†1]	1996	BioFreedom™* DCS	✓	None	80%	38 mm	46%	53%	26%
Onyx ONE Clear analysis[2]	1506	Objective performance criteria (OPC)	✗	None	79%	37 mm	50%	49%	26%
XIENCE 28 study[3]	1392	Single-arm Historical control (XIENCE V USA Study 2008–2011)	✗	Excluded: Left main CTO ISR Overlapping stents SVG	36%	27 mm	Not reported	34% No STEMI	15.8%
POEM (Synergy™* Stent)[4]	443	Objective performance criteria	✗	None	49%	24 mm	Not reported	41%	Not reported

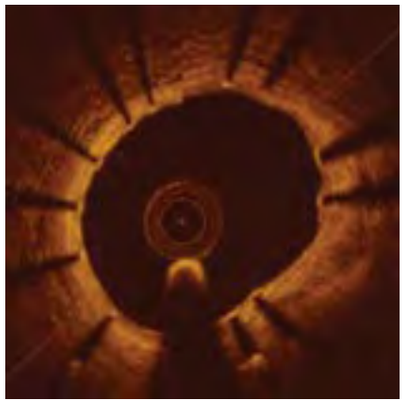
*Third-party brands are trademarks of their respective owners.
†Results include the Resolute Onyx DES treated arm.
[1] Windecker S, et al. *N Engl J Med*. 2020;382:1208-1218.
[2]Kandzari D, et al. *Circ Cardiovasc Interv*. 2020;13: e009565.
[3]Mehran R, et al. The Xience Short DAPT Program: Xience 90/28. Evaluating the Safety of 3-month and 1-month DAPT in HBR Patients. Presented at TCT Congress 2020.
[4] Stefanini G, et al. The POEM Study: One-Month DAPT in HBR Patients. Presented at PCR 2021.

Why Resolute Onyx™ DES for HBR patients on 1-month DAPT?

Resolute Onyx DES is different by design to promote fast healing[1]



Less fluorescence (red) is better



Single-wire design provides a fluid range of motion and the conformability needed for superior strut apposition[2]

BioLinx™ biocompatible polymer provides superior thromboresistance[3]

Fast healing occurs as evidenced by nearly 90% strut coverage at 30 days,[1] providing the option to shorten DAPT

*Third-party brands are trademarks of their respective owners.

[1] Roleder T, et al. *Postepy Kardiol Interwencyjnej.* 2019;15:143-150.
[2] Data on file at Medtronic.
[3] Jinnouchi H, et al. *Int J Cardiol.* 2021;327:52-57.

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