# ONYX ONE CLINICAL SUMMARY

## BACKGROUND



## CLINICAL DATA



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# ONYX ONE OVERVIEW

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

## 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

**AF SUBGROUP[4]**
TCT 2020

**COMPLEX PCI SUBGROUP[5]**
TCT 2020

**SEX SUBGROUP[6]**
SCAI 2021

**DIABETIC SUBGROUP[7]**
PCR 2021

## 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**

[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 ESC2020.
[4]Pasupati S, et al. Ischemic and Bleeding Outcomes in Patients With vs. Without AF. Presented at TCT2020.
[5]Kandzari D, et al. Complex PCI with 1-month DAPT in HBR Patients: Presented at TCT2020.
[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.

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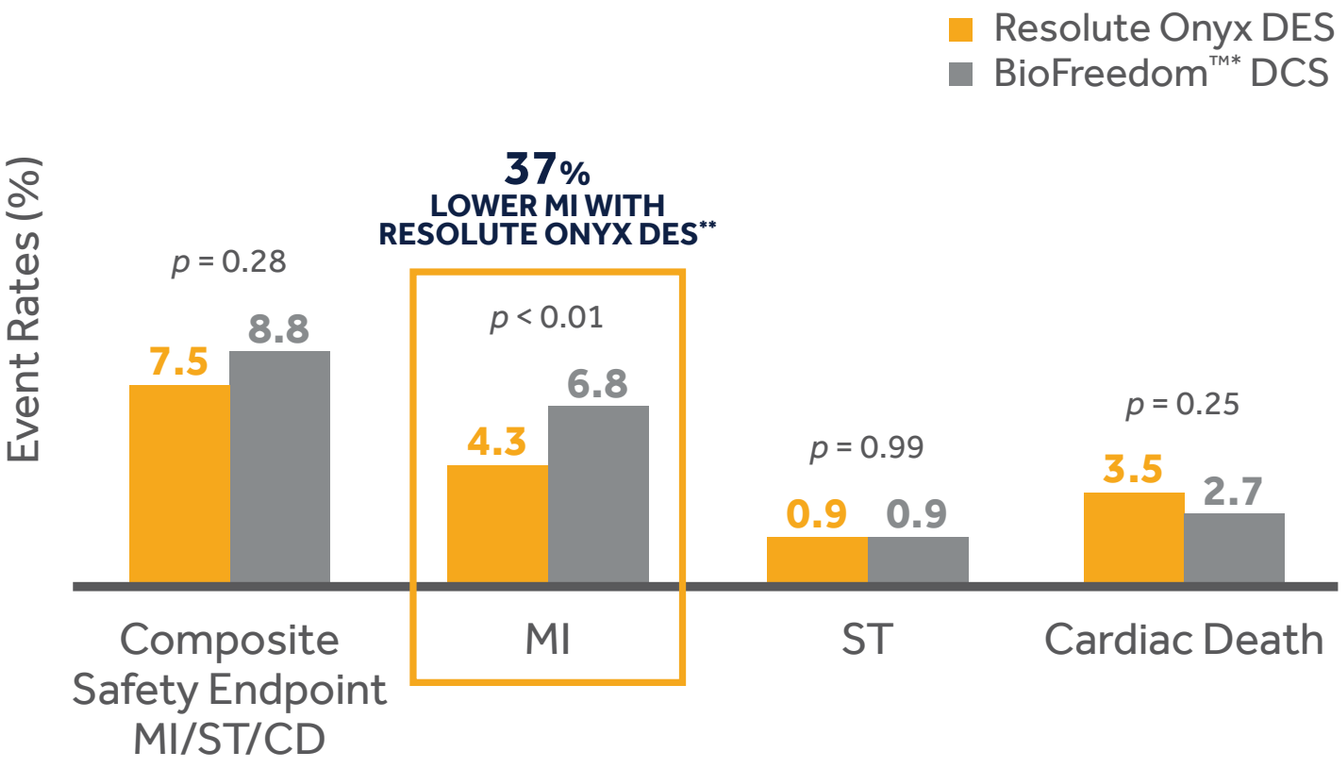
# ONYX ONE GLOBAL TRIAL 1-YEAR RESULTS

**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.

- 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 is the first DES CE indicated for 1-month DAPT in HBR patients based on the results from this study


Polymer-based or Polymer-free Stents in Patients at High Bleeding Risk

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

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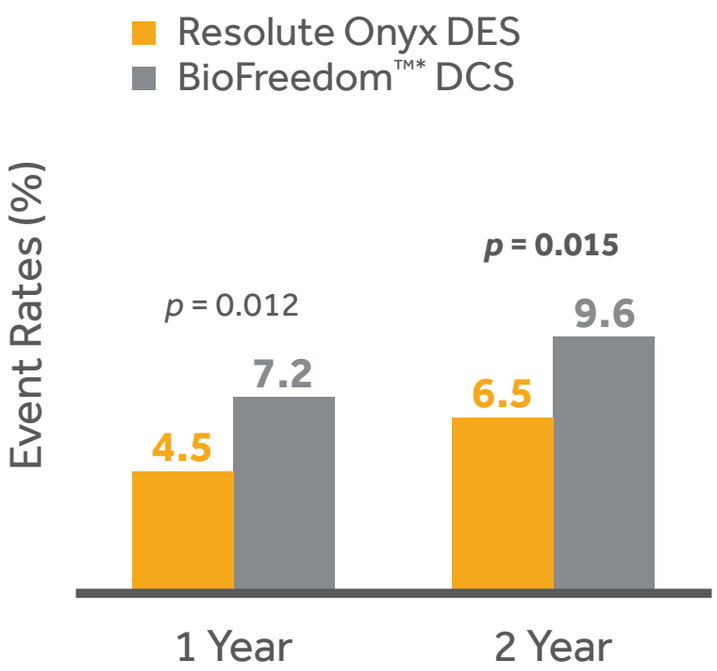
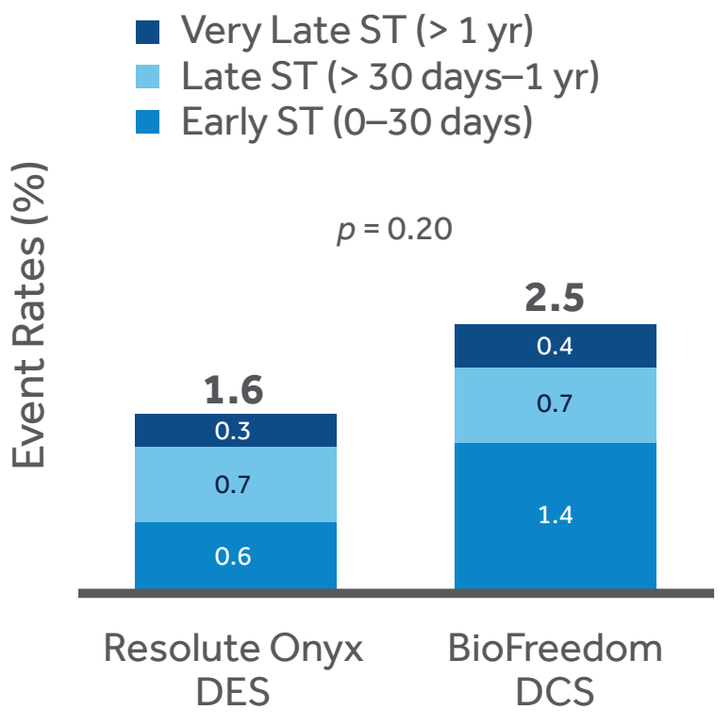
# ONYX ONE GLOBAL TRIAL 2-YEAR RESULTS

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

## SIGNIFICANTLY LOWER SPONTANEOUS MI WITH RESOLUTE ONYX DES†




## LOW STENT THROMBOSIS CONFIRMED AT 2-YEAR FOLLOW-UP†




- 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%) ($p = 0.035$)

*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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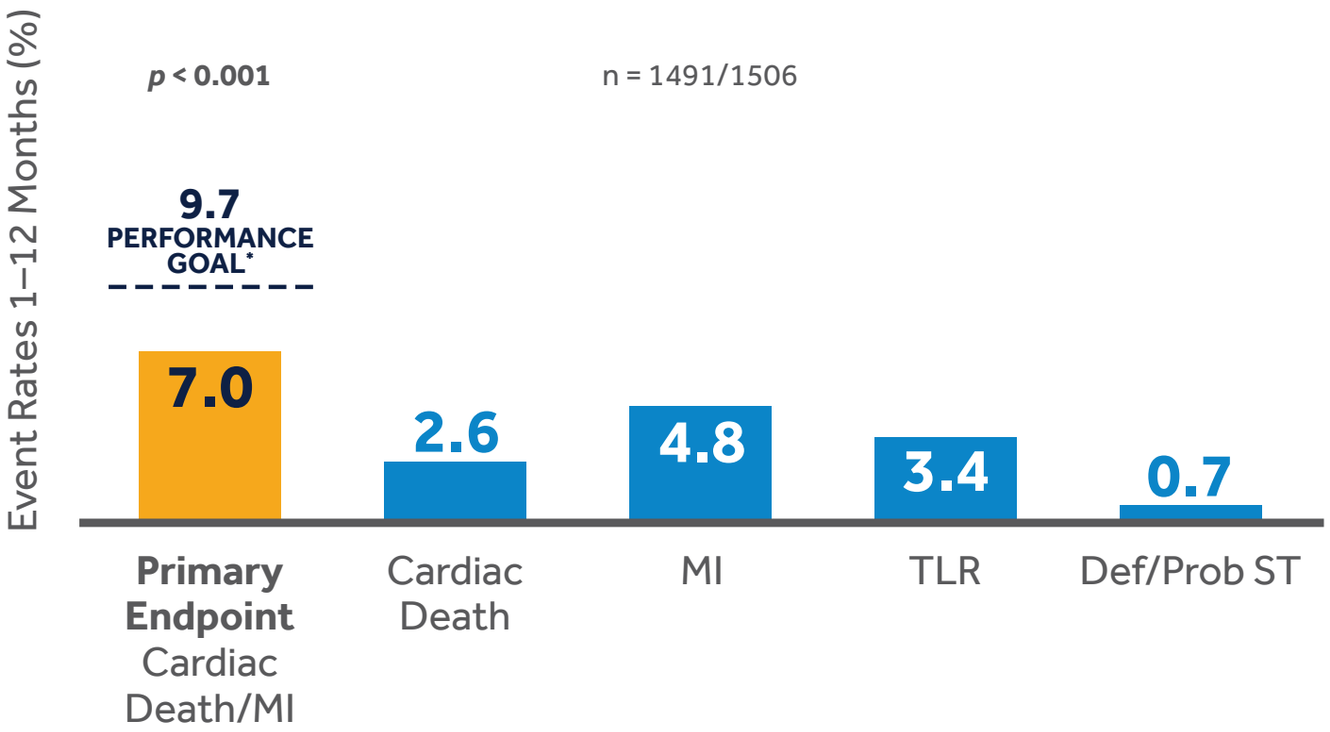
# ONYX ONE CLEAR ANALYSIS

**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.

- 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 one 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

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

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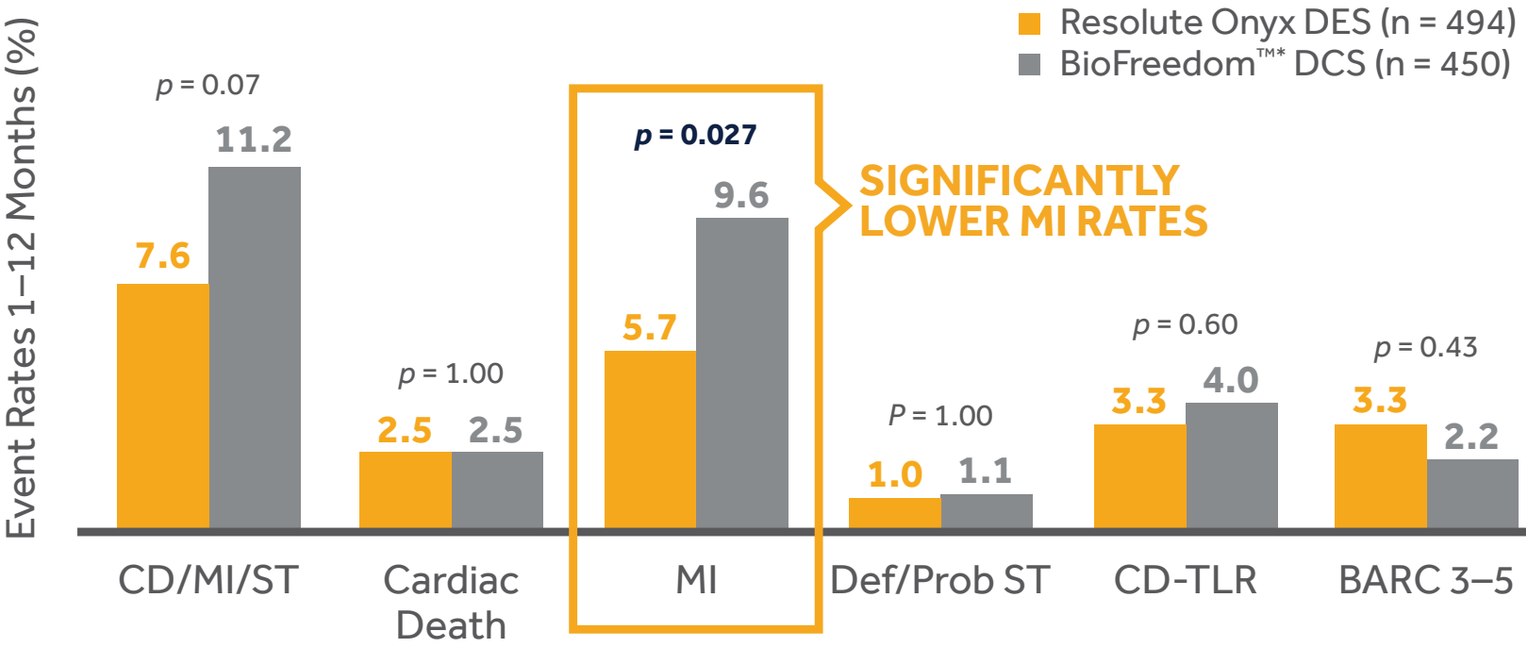
# ACUTE CORONARY SYNDROME (ACS) SUBANALYSIS RESULTS

**Reinforced 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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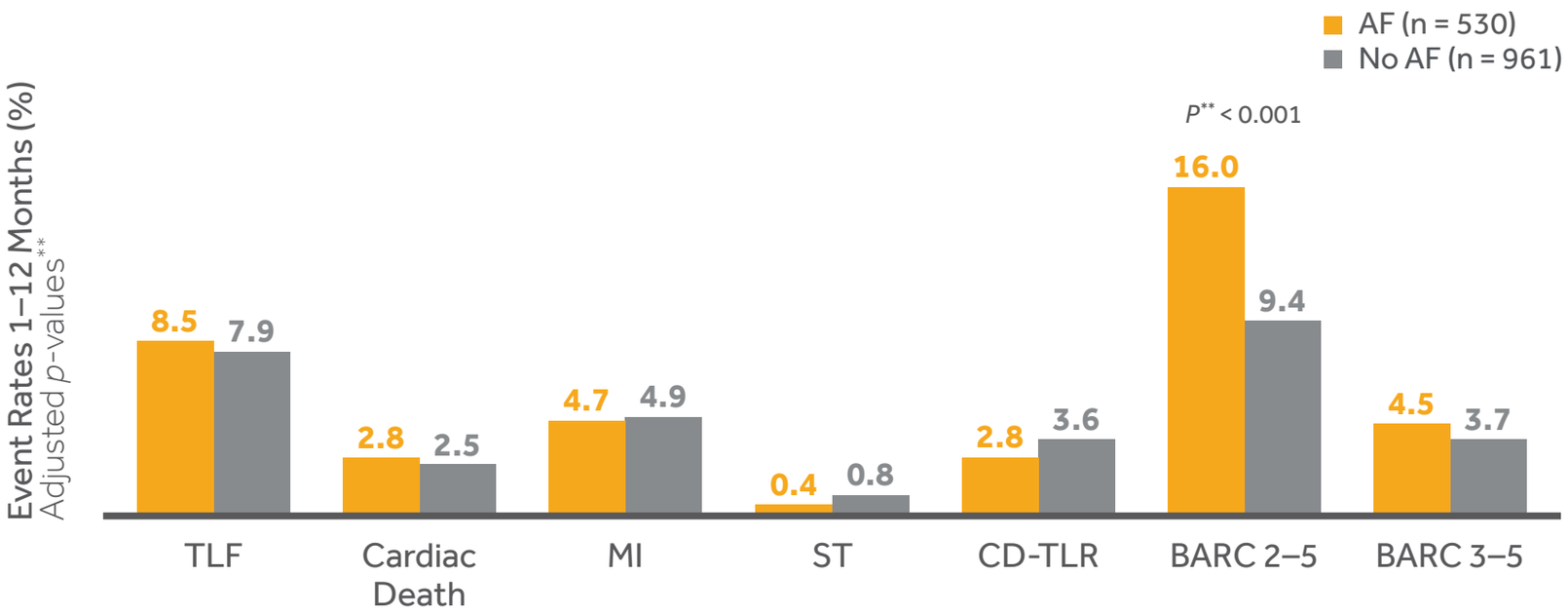
# ATRIAL FIBRILLATION (AF) SUBANALYSIS

**Reinforced 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)†




*Based on post-hoc analysis. Results not adjusted for multiple comparisons.
†Endpoints were not powered.
**P-values adjusted by propensity scores for baseline differences; 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.

- 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

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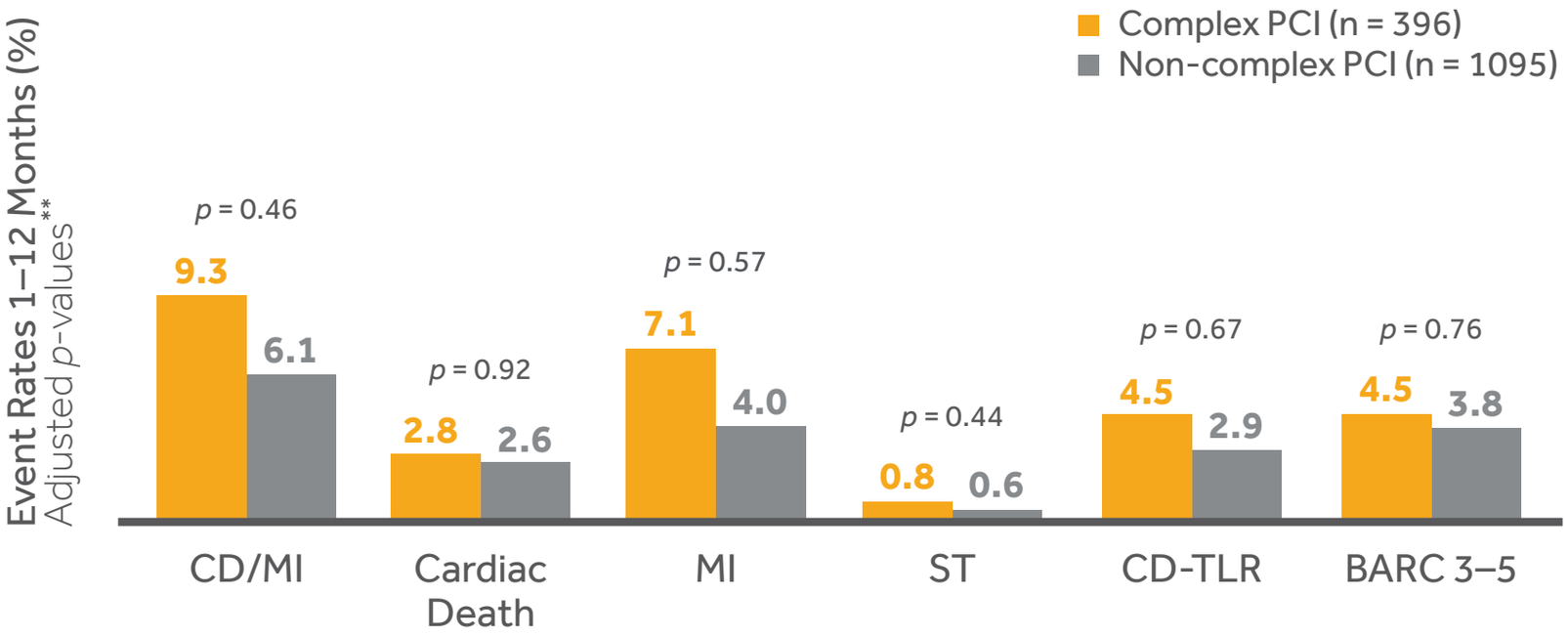
# COMPLEX PCI SUBANALYSIS

**Reinforced 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†




*Based on post-hoc analysis. Results not adjusted for multiple comparisons.
†Endpoints were not powered.
**Propensity score adjusted *p*-values for differences in baseline characteristics.
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.

- 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†
  - Chronic total occlusion
- 1.6 high bleeding risk criteria per patient
- 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% $p < 0.001$)

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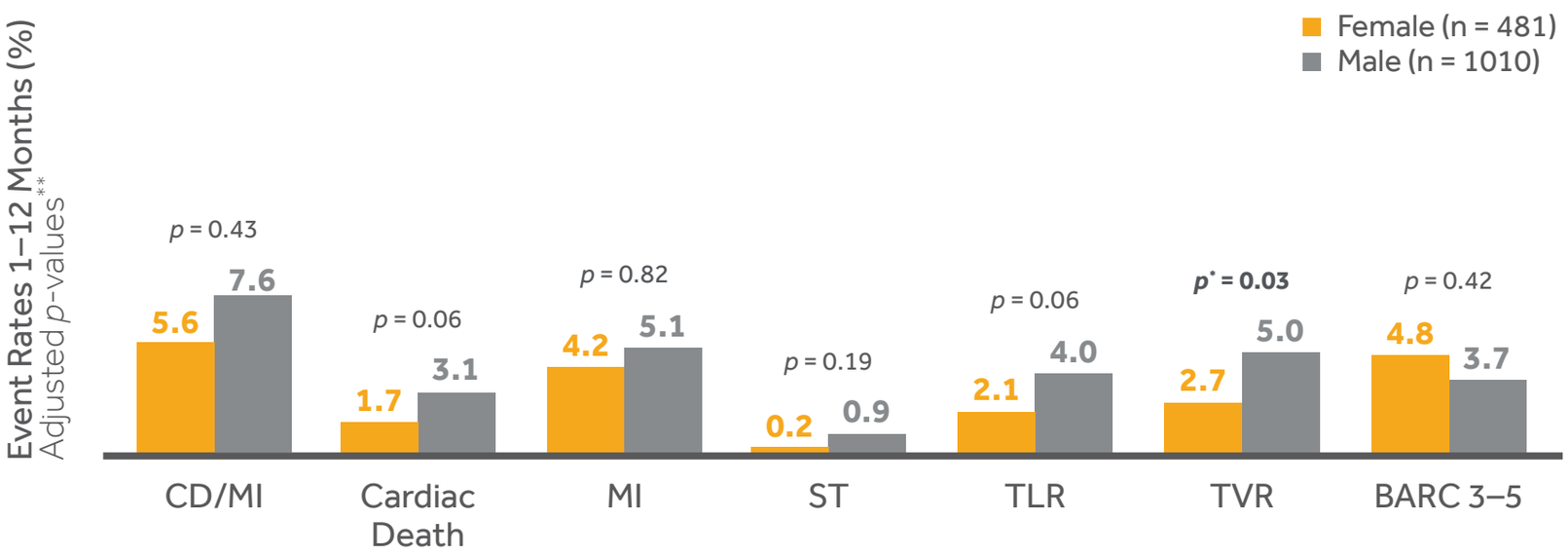
# SEX SUBANALYSIS

**Reinforced 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†




*Results not adjusted for multiple comparisons.
†Endpoints were not powered.
**Propensity score adjusted *p*-values 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.

- 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)

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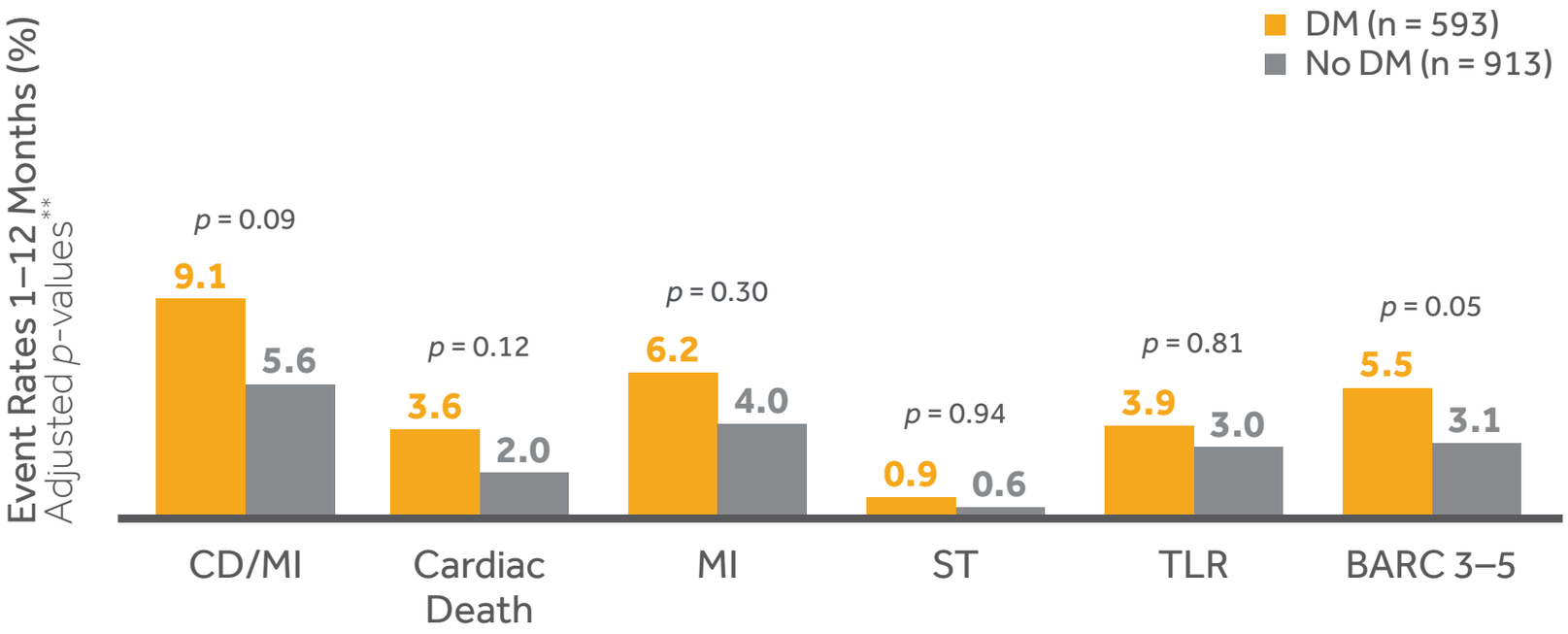
# DIABETIC SUBANALYSIS

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

## NO DIFFERENCE IN SAFETY AND EFFICACY OBSERVED IN DM VS. NO-DM GROUPS DESPITE INCREASED LESION COMPLEXITY†




*Results not adjusted for multiple comparisons.
†Endpoints were not powered.
**Propensity score adjusted *p*-values 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.

- 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

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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% | 26.3% |
| **XIENCE 28 STUDY**[3] | 1392 | Single-arm<br><br>Historical Control (XIENCE V USA Study 2008–2011) | ✗ | **Excluded:**<br>Left main<br>CTO<br>ISR<br>Overlapping stents<br>SVG | 36% | 27 mm | Not Reported | 34%<br>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.

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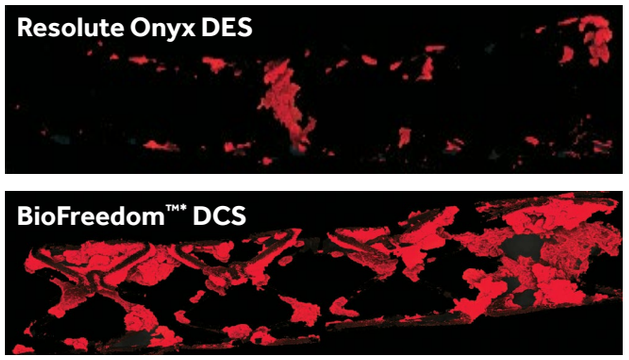
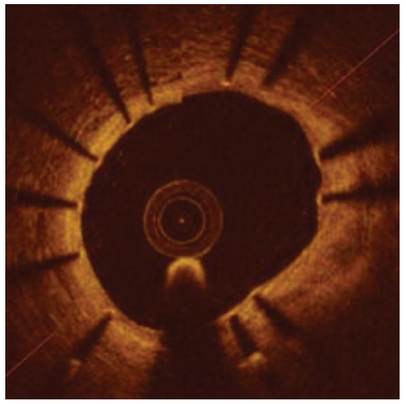
# WHY RESOLUTE ONYX™ DES FOR HBR PATIENTS ON 1-MONTH DAPT?

## RESOLUTE ONYX DES IS DIFFERENT BY DESIGN TO PROMOTE FAST HEALING




Less fluorescence (red) is better



**Single-wire design** provides a fluid range of motion and the conformability needed for superior strut apposition[1]

**BioLinx™ biocompatible polymer** provides superior thromboresistance[2]

**Fast healing** occurs as evidenced by nearly 90% strut coverage at 30 days,[3] **providing the option to shorten DAPT**

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

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

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