1-MONTH DAPT EVIDENCE IN COMPLEX PATIENTS

Onyx ONE Month DAPT Program
Evaluating Resolute Onyx™ DES in ~1,700 patients with 1-month DAPT.†

Resolute Onyx DES

Medtronic is committed to developing additional evidence to help guide dual antiplatelet therapy treatment decisions, which are best made on an individual basis and should integrate current guidelines, clinical judgment, assessment of the benefit/risk ratio, and patient preference. Resolute Onyx DES is not currently indicated for high bleeding risk patients on 1-month DAPT.

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ADVANCING DAPT EVIDENCE

Medtronic is committed to developing additional evidence to help guide DAPT decisions.

High bleeding risk (HBR) patients are a large, growing, complex population that historically had little evidence to support treatment decisions. HBR patients often have more complex disease than all-comer patients. For these reasons, Medtronic initiated the Onyx ONE Month DAPT Program.

Onyx ONE Month DAPT Program
Evaluating Resolute Onyx DES in ~1,700 patients with 1-month DAPT.

ONYX ONE GLOBAL STUDY
First prospective, randomized, 1-month DAPT trial comparing a DES to a DES in HBR patients.

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ONYX ONE CLEAR STUDY
First study in the U.S. and Japan evaluating 1-month DAPT duration in HBR patients with a current DES.

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ONYX ONE MONTH DAPT PROGRAM
The most robust clinical program studying 2,700 highly complex HBR patients with 1-month DAPT.

ONYX ONE MONTH DAPT PROGRAM

The most robust clinical program studying **2,700** highly complex HBR patients with 1-month DAPT.

COMPLEX HBR PATIENT POPULATION

THE ONYX ONE MONTH DAPT PROGRAM ENROLLED HIGHLY COMPLEX HIGH BLEEDING RISK PATIENTS, REFLECTIVE OF A REAL-WORLD PATIENT POPULATION.[1]

		NO VESSEL OR LESION LIMITATIONS			REAL-WORLD PATIENTS			BROAD HBR INCLUSION CRITERIA**[1]	
		B2/C LESIONS	AVERAGE STENTED LENGTH	MOD/SEV CALCIFIED LESIONS	AVERAGE AGE	DIABETES	PRIOR REVASC.	HBR CRITERIA PER PATIENT	PATIENTS HAVING TWO OR MORE HBR CRITERIA
ONYX ONE GLOBAL STUDY	Resolute Onyx DES Arm (1,003 patients)	80%	38 mm	46%	74	39%	31%	1.6	46%
ONYX ONE CLEAR STUDY	"Clear" patients treated with Resolute Onyx DES (1,506)	79%	37 mm	50%	74	39%	36%	1.6	44%

HBR INCLUSION CRITERIA[1]

PATIENTS MEETING CRITERIA	RESOLUTE ONYX DES (N = 1,506) ONYX ONE CLEAR STUDY	RESOLUTE ONYX DES (N = 1,003) ONYX ONE GLOBAL STUDY
Elderly (age ≥ 75 yr)	59.0	61.1
OAC	41.0%	38.5%
Anemia or transfusion	14.4%	15.6%
Renal failure	12.5%	14.3%
Active or recent cancer	7.4%	8.5%
Planned surgery	6.6%	5.6%
Expected DAPT noncompliance	4.2%	3.9%
Stroke < 1 yr	2.6%	2.9%
Hospital for bleeding	2.8%	3.0%
Long-term NSAID or steroids	3.1%	2.4%
Previous intracranial bleed	1.7%	2.0%
Thrombocytopenia	1.7%	1.5%
Severe liver disease	0.9%	0.8%

ONYX ONE GLOBAL STUDY + **ONYX ONE CLEAR STUDY** = **ONYX ONE MONTH DAPT PROGRAM**

ONYX ONE GLOBAL STUDY

First prospective, randomized, 1-month DAPT trial comparing a **DES to a DES** in HBR patients.

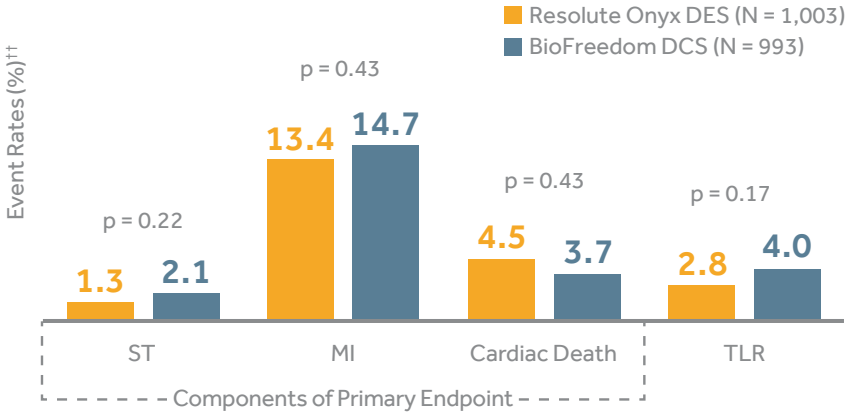
TRIAL DESIGN

HBR patients undergoing PCI in a prospective, randomized, clinical trial, DES vs. DES

- **Resolute Onyx DES** (N = 1,003)
- **BioFreedom DCS** (N = 993)

ONE-YEAR RESULTS

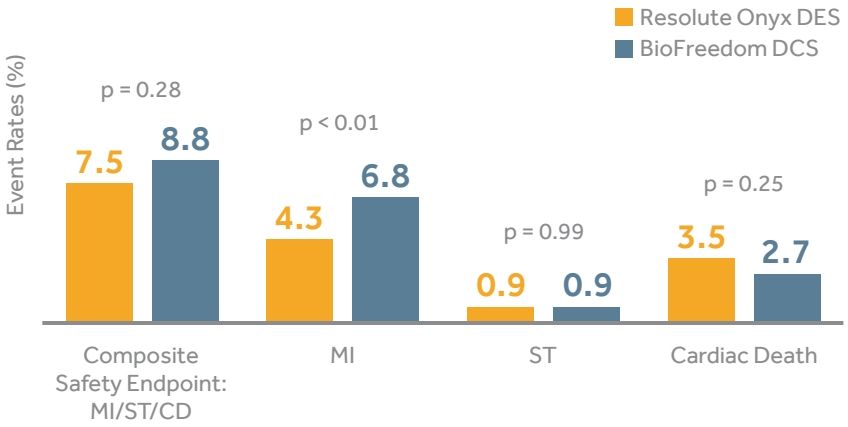
PRIMARY ENDPOINT MET WITH RESOLUTE ONYX DES (17.1%) NONINFERIOR TO BIOFREEDOM™* DCS (16.9%)[2]



RESULTS PUBLISHED IN ***THE NEW ENGLAND JOURNAL OF MEDICINE***

LANDMARK ANALYSIS AFTER DAPT DISCONTINUATION

LANDMARK ANALYSIS AFTER DAPT DISCONTINUATION[2] IN A HIGHLY COMPLEX PATIENT POPULATION***



ONYX ONE CLEAR STUDY

First study in the **United States and Japan** evaluating 1-month DAPT duration in HBR patients with a current DES.

TRIAL DESIGN

"Clear" HBR patients undergoing PCI in a prospective, multicenter, single-arm trial

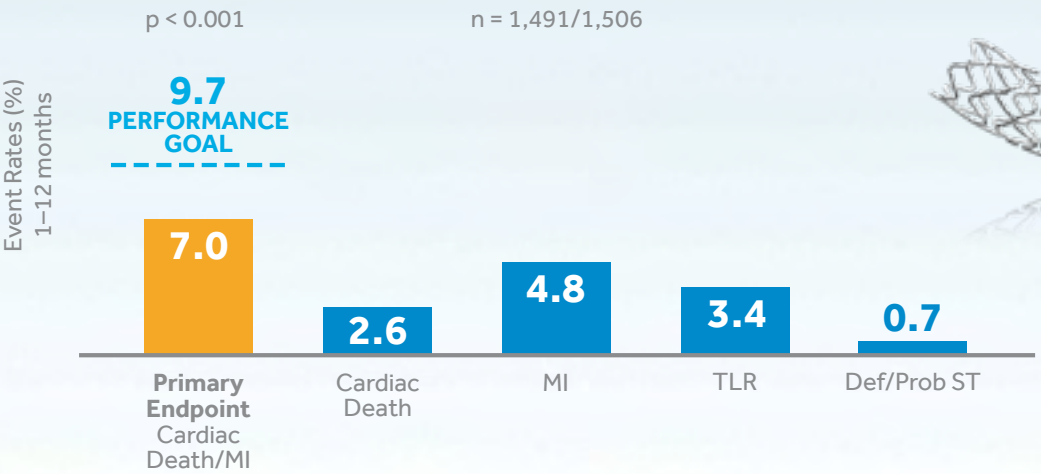
Resolute Onyx DES with 1-mo DAPT
United States and Japan (n = ~600)
Onyx ONE Global Study (n = ~900)
(N = ~1,500)

Performance Goal

"Clear" patients are defined as being event-free and DAPT-adherent for the first 30 days post-procedure. Events include spontaneous MI, repeat revascularization, stroke, stent thrombosis, and death through 1 month.

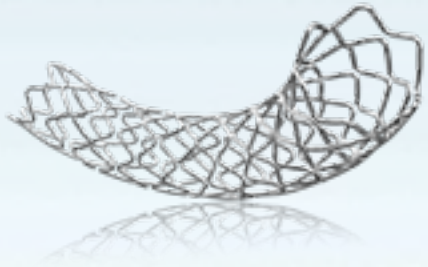
PRIMARY ENDPOINT RESULTS

RESOLUTE ONYX DES BEAT PERFORMANCE GOAL FOR CARDIAC DEATH AND MI



Performance goal derived from contemporary 1-month DAPT trials.[†††]

THE ONYX ONE CLEAR ANALYSIS showed 7.0% cardiac death or myocardial infarction at one year, **beating the performance goal of 9.7%.**[3]



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*Third party brands are trademarks of their respective owners.
†Current ACC/AHA guidelines regarding DAPT duration following PCI: Per ACC/AHA guidelines, a daily aspirin dose of 81 mg is recommended indefinitely after PCI. A P2Y12 platelet inhibitor should be given daily for at least 6 months in stable ischemic heart disease (SIHD) patients and for at least 12 months in patients with acute coronary syndrome (ACS). Consistent with the 2016 ACC/AHA guidelines, longer duration of DAPT may be considered in any patients at higher ischemic risk with lower bleeding risk. In patients at higher risk of bleeding, DAPT discontinuation may be reasonable after 3 months in stable SIHD patients or 6 months in ACS patients. Decisions about duration of DAPT are best made on an individual basis and should integrate clinical judgment, assessment of the benefit/risk ratio, and patient preference. Physicians should consider all of the available evidence on DAPT to make the most appropriate decisions for each of their patients. Resolute Onyx DES is not currently indicated for high bleeding risk patients on 1-month DAPT.
**Matching LEADERS FREE inclusion criteria.
††Endpoints were not separately powered.
***Post-hoc analyses were not powered. From 1 month to 1 year.
†††ZEUS, LEADERS FREE, and SENIOR trials.

[1] Kedhi E, Latib A, Abizaid A, et al. Rationale and design of the Onyx ONE global randomized trial: A randomized controlled trial of high bleeding risk patients after stent placement with 1 month of dual antiplatelet therapy. *Am Heart J.* August 2019;214:134-141.
[2] Windecker S, Latib A, Kedhi E, et al. Polymer-based or Polymer-free Stents in Patients at High Bleeding Risk. *N Engl J Med.* March 26, 2020;382(13):1208-1218.
[3] Kirtane A, et al. One Month Dual Antiplatelet Therapy in High Bleeding Risk Patients: Primary Results of Onyx ONE Clear. Presented online at ACC 2020.

Resolute Onyx™ Zotarolimus-eluting Coronary Stent System

Indications

The Resolute Onyx™ Zotarolimus-eluting Coronary Stent System is indicated for improving coronary luminal diameters in patients, including those with diabetes mellitus, with symptomatic ischemic heart disease due to *de novo* lesions of length ≤ 35 mm in native coronary arteries with reference vessel diameters of 2.0 mm to 5.0 mm. In addition, the Resolute Onyx™ Zotarolimus-eluting Coronary Stent System is indicated for treating *de novo* chronic total occlusions.

Contraindications

The Resolute Onyx™ Zotarolimus-eluting Coronary Stent System is contraindicated for use in: ▪Patients with a known hypersensitivity or allergies to aspirin, heparin, bivalirudin, clopidogrel, prasugrel, ticagrelor, ticlopidine, drugs such as zotarolimus, tacrolimus, sirolimus, everolimus, or similar drugs or any other analogue or derivative ▪Patients with a known hypersensitivity to the cobalt-based alloy (cobalt, nickel, chromium, and molybdenum) or platinum-iridium alloy ▪Patients with a known hypersensitivity to the BioLinx™ polymer or its individual components

Coronary artery stenting is contraindicated for use in: ▪Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated ▪Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or stent delivery system

Warnings

▪Please ensure that the inner package has not been opened or damaged as this would indicate the sterile barrier has been breached. ▪The use of this product carries the same risks associated withcoronary artery stent implantation procedures, which include subacute and late vessel thrombosis, vascular complications, and/or bleeding events. ▪This product should not be used in patients who are not likely to comply with the recommended antiplatelet therapy.

Precautions

▪Only physicians who have received adequate training should perform implantation of the stent. ▪Subsequent stent restenosis or occlusion may require repeat catheter-based treatments (including balloon dilatation) of the arterial segment containing the stent. The long-term outcome following repeat catheter-based treatments of previously implanted stents is not well characterized. ▪The risks and benefits of the stent implantation should be assessed for patients with a history of severe reaction to contrast agents. ▪Do not expose or wipe the product with organic solvents such as alcohol. ▪The use of a drug-eluting stent (DES) outside of the labeled indications, including use in patients with more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death. ▪Care should be taken to control the position of the guide catheter tip during stent delivery, stent deployment, and balloon withdrawal. Before withdrawing the stent delivery system, confirm complete balloon deflation using fluoroscopy to avoid arterial damage caused by guiding catheter movement into the vessel. ▪Stent thrombosis is a low-frequency event that is frequently associated with myocardial infarction (MI) or death. Data from the RESOLUTE clinical trials have been prospectively evaluated and adjudicated using the definition developed by the Academic Research Consortium (ARC).

The safety and effectiveness of the Resolute Onyx™ stent have not yet been established in the following patient populations: ▪Patients with target lesions that were treated with prior brachytherapy or the use of brachytherapy to treat in-stent restenosis of a Resolute Onyx™ stent ▪Women who are pregnant or lactating ▪Men intending to father children ▪Pediatric patients ▪Patients with coronary artery reference vessel diameters of < 2.0 mm or > 5.0 mm ▪Patients with evidence of an acute ST-elevation MI within 72 hours of intended stent implantation ▪Patients with vessel thrombus at the lesion site ▪Patients with lesions located in a saphenous vein graft, in the left main coronary artery, ostial lesions, or bifurcation lesions ▪Patients with diffuse disease or poor flow distal to identified lesions ▪Patients with three-vessel disease

The safety and effectiveness of the Resolute Onyx™ stent have not been established in the cerebral, carotid, or peripheral vasculature.

Potential Adverse Events

Other risks associated with using this device are those associated with percutaneous coronary diagnostic (including angiography and IVUS) and treatment procedures. These risks (in alphabetical order) may include but are not limited to: ▪Abrupt vessel closure ▪Access site pain, hematoma, or hemorrhage ▪Allergic reaction (to contrast, antiplatelet therapy, stent material, or drug and polymer coating) ▪Aneurysm, pseudoaneurysm, or arteriovenous fistula (AVF) ▪Arrhythmias, including ventricular fibrillation ▪Balloon rupture ▪Bleeding ▪Cardiac tamponade ▪Coronary artery occlusion, perforation, rupture, or dissection ▪Coronary artery spasm ▪Death ▪Embolism (air, tissue, device, or thrombus) ▪Emergency surgery: peripheral vascular or coronary bypass ▪Failure to deliver the stent ▪Hemorrhage requiring transfusion ▪Hypotension/hypertension ▪Incomplete stent apposition ▪Infection or fever ▪MI ▪Pericarditis ▪Peripheral ischemia/peripheral nerve injury ▪Renal failure ▪Restenosis of the stented artery ▪Shock/pulmonary edema ▪Stable or unstable angina ▪Stent deformation, collapse, or fracture ▪Stent migration or embolization ▪Stent misplacement ▪Stroke/transient ischemic attack ▪Thrombosis (acute, subacute, or late)

Adverse Events Related to Zotarolimus

Patients' exposure to zotarolimus is directly related to the total amount of stent length implanted. The actual side effects/complications that may be associated with the use of zotarolimus are not fully known. The adverse events that have been associated with the intravenous injection of zotarolimus in humans include but are not limited to: ▪Anemia ▪Diarrhea ▪Dry skin ▪Headache ▪Hematuria ▪Infection ▪Injection site reaction ▪Pain (abdominal, arthralgia, injection site) ▪Rash

Please reference appropriate product *Instructions for Use* for more information regarding indications, warnings, precautions, and potential adverse events.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

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