Medtronic

Endeavor® Sprint

ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM

ENDEAVOR III and ENDEAVOR Pooled Analysis at 5 Years – ACC 2010

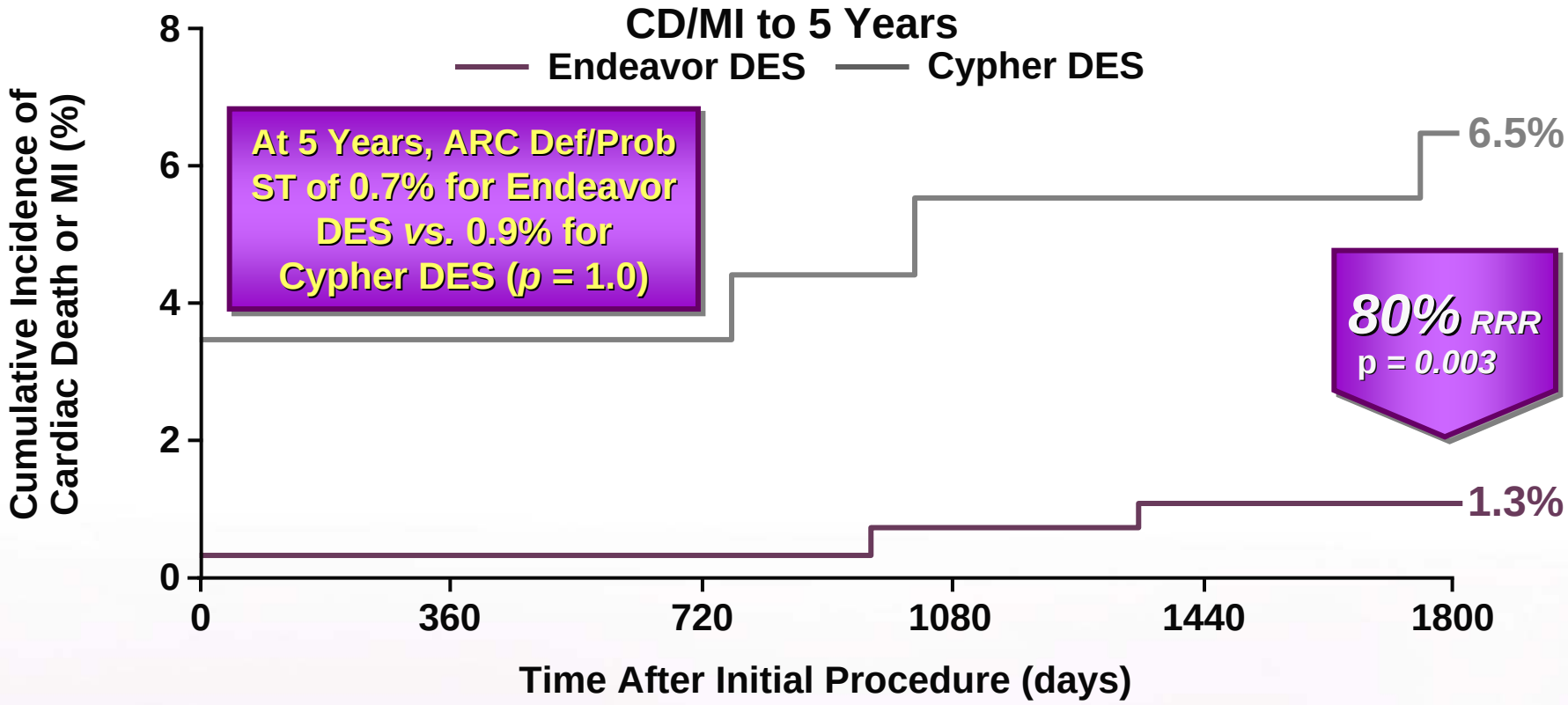
Healing First, Results That Last

ENDEAVOR III – Significant Differences At 5 Years

- **Significant differences in safety and composite endpoints:**
  - **80% relative risk reduction in CD/MI (Endeavor DES 1.3% *vs.* Cypher DES 6.5%, *p* = 0.003[1])**
  - **37% relative risk reduction in MACE (Endeavor DES 14.0% *vs.* Cypher DES 22.2%, *p* = 0.0495[2])**
- **Confirmation of late TLR catch up with Cypher DES**
  - **86% increase in TLR with Cypher DES *vs.* 21% increase with Endeavor DES from years 1–5 drives similar TLR rate at 5 years (Endeavor DES 8.0% *vs.* Cypher DES 6.5%, *p* = 0.547[1])**
- **Primary endpoint: In-segment late lumen loss by QCA at 8 months, 0.36 for Endeavor *vs.* 0.13 for Cypher (p<0.001)**

[1] *p*-Value was calculated by logrank test. p-Values are unadjusted for multiple comparisons.
[2] *p*-Value was calculated by Fisher Exact test.
ENDEAVOR III was not specifically designed or powered to individually compare CD/MI, MACE, or TLR.
MACE is composed of Death, MI, Emergent CABG, TLR.

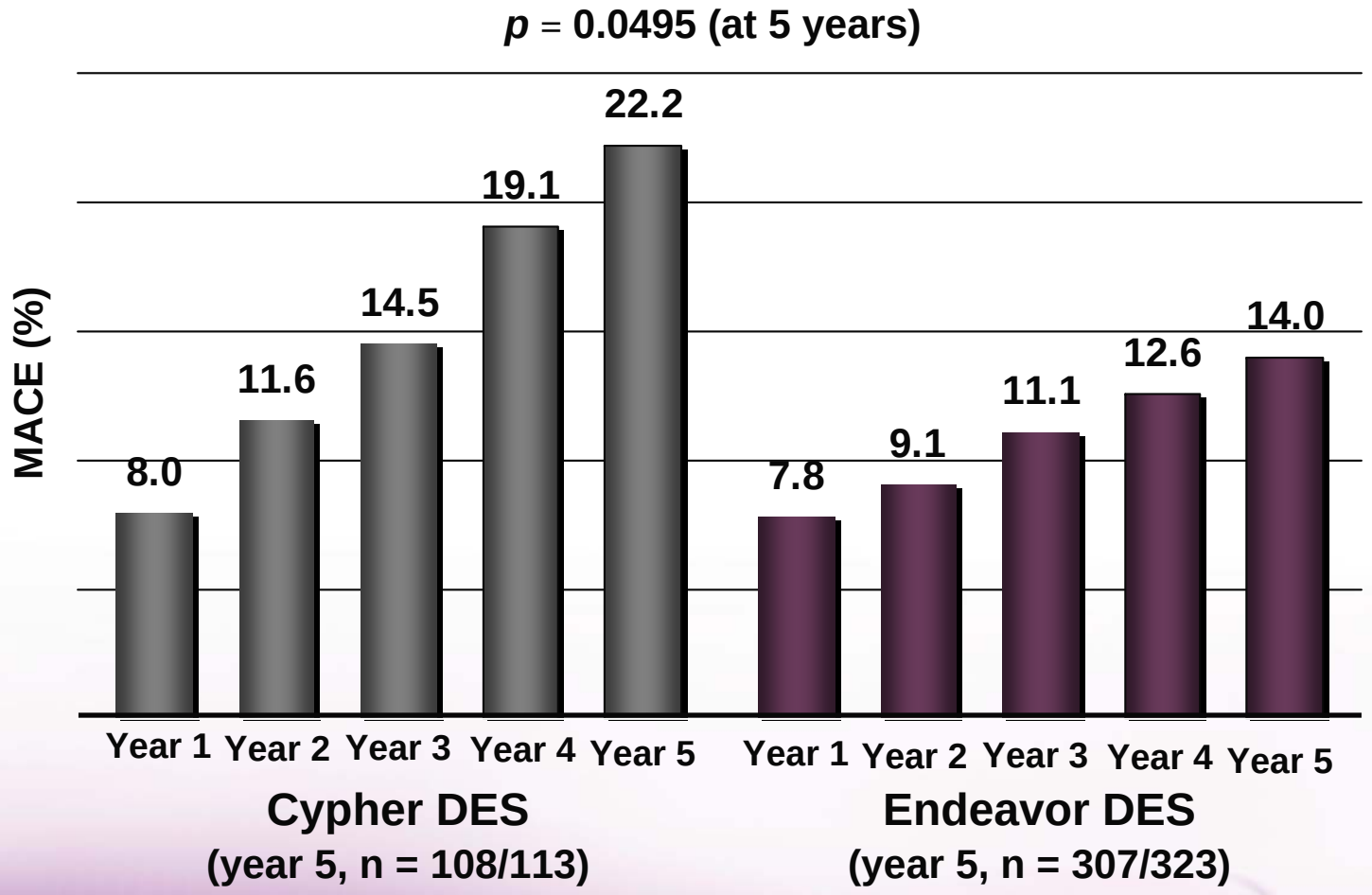
80% Significant Risk Reduction in Cardiac Death/MI



Endeavor	323	321	314	306	298	290
CI (%)	*0.62*	*0.62*	*0.62*	*0.95*	*1.29*	*1.29*
Cypher	113	109	107	103	98	94
CI (%)	*3.54*	*3.54*	*3.54*	*5.45*	*5.45*	*6.50*

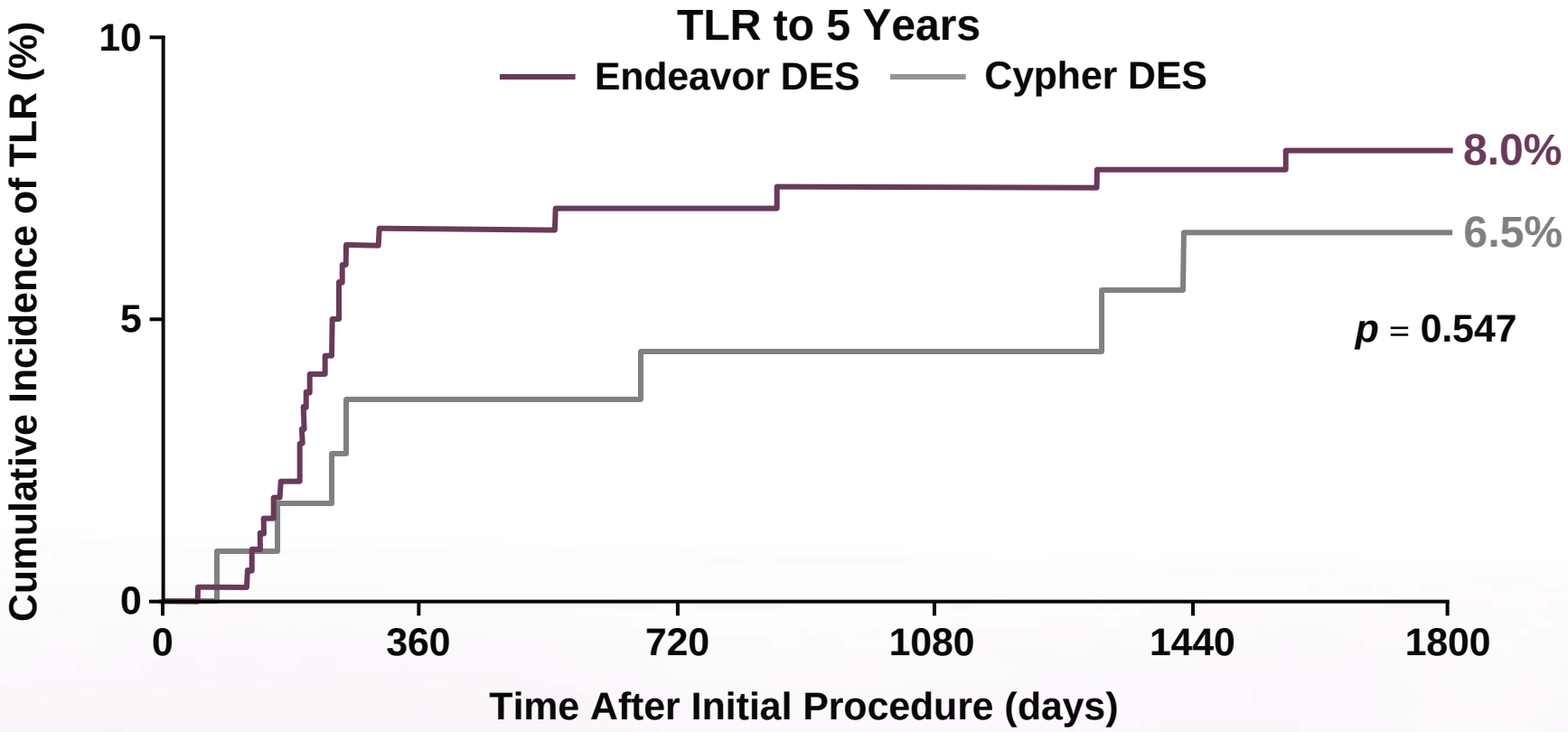
p-Values are unadjusted for multiple comparisons. *p*-Values were calculated by logrank test.
ENDEAVOR III was not specifically designed or powered to individually compare CD/MI or ST. RRR = relative risk reduction.
ENDEAVOR III primary endpoint: In-segment late lumen loss by QCA at 8 months. 0.36 for Endeavor vs 0.13 for Cypher (p<0.001).

37% Significant Risk Reduction in MACE



p-Value was calculated by Fisher Exact test. *p*-Values for outcome differences are unadjusted for multiple comparisons.
ENDEAVOR III was not specifically designed or powered to individually compare MACE.
MACE is composed of Death, MI, Emergent CABG, TLR.
ENDEAVOR III primary endpoint: In-segment late lumen loss by QCA at 8 months. 0.36 for Endeavor vs 0.13 for Cypher (p<0.001).

Endeavor DES Displayed Low And Sustained TLR Rates



Endeavor	323	323	280	272	263	257
CI (%)	*0.0*	*6.6*	*6.9*	*7.3*	*7.7*	*8.0*
Cypher	113	113	107	101	97	91
CI (%)	*0.0*	*3.5*	*4.5*	*4.5*	*6.5*	*6.5*

p-Values are unadjusted for multiple comparisons.
p-Values were calculated by logrank test.
ENDEAVOR III was not specifically designed or powered to individually compare TLR.
ENDEAVOR III primary endpoint: In-segment late lumen loss by QCA at 8 months. 0.36 for Endeavor vs 0.13 for Cypher (p<0.001).

ENDEAVOR III – Significant Differences At 5 Years

- **Significant differences in safety and composite endpoints:**
  - **80% relative risk reduction in CD/MI (Endeavor DES 1.3% *vs.* Cypher DES 6.5%, *p* = 0.003[1])**
  - **37% relative risk reduction in MACE (Endeavor DES 14.0% *vs.* Cypher DES 22.2%, *p* = 0.0495[2])**
- **Confirmation of late TLR catch up with Cypher DES**
  - **86% increase in TLR with Cypher DES *vs.* 21% increase with Endeavor DES from years 1–5 drives similar TLR rate at 5 years (Endeavor DES 8.0% *vs.* Cypher DES 6.5%, *p* = 0.547[1])**
- **Primary endpoint: In-segment late lumen loss by QCA at 8 months, 0.36 for Endeavor *vs.* 0.13 for Cypher (p<0.001)**

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MACE is composed of Death, MI, Emergent CABG, TLR.

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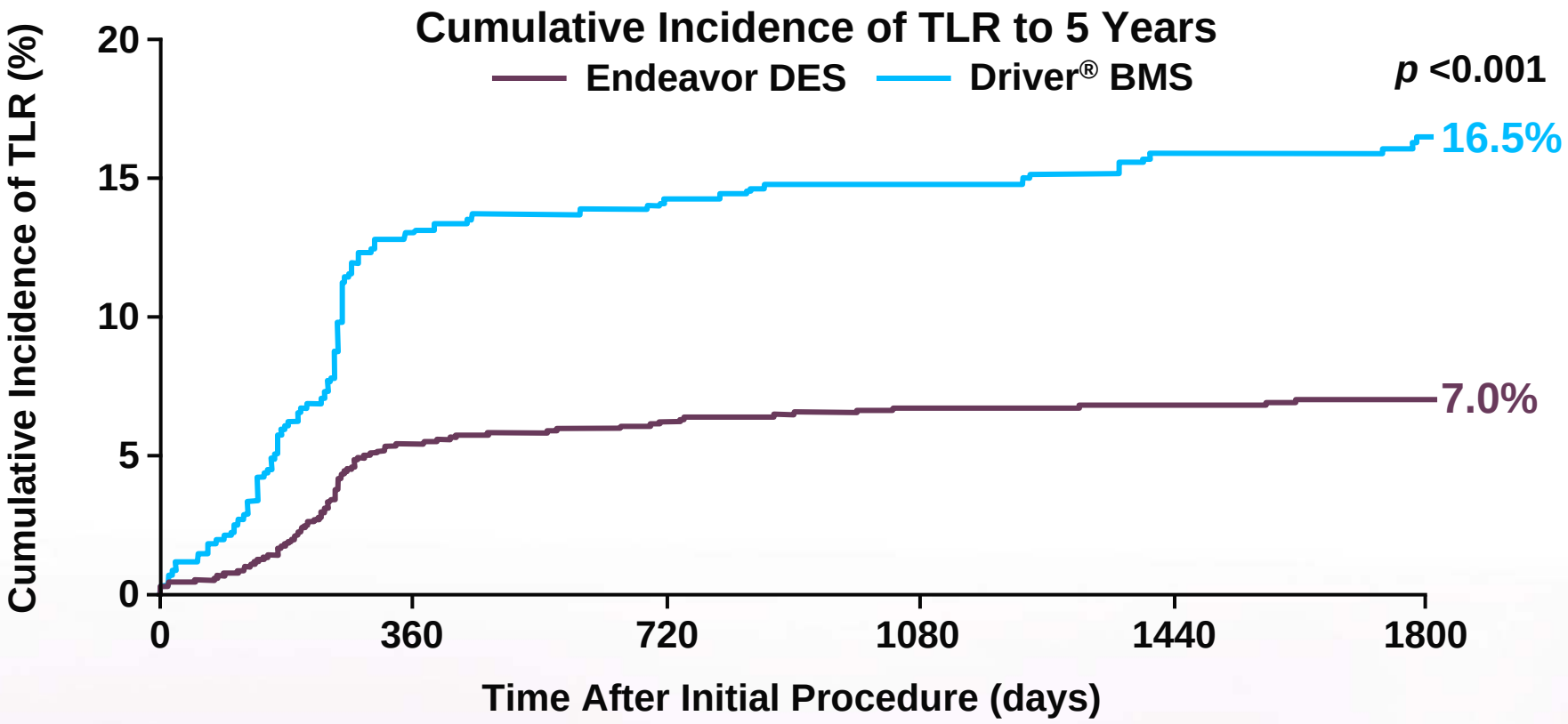
ENDEAVOR III Consistent With ENDEAVOR Pooled Analysis

ENDEAVOR III: Results Consistent with The Pooled Analysis

- **Endeavor has robust, long-term clinical proof:**
  - **More than 2100 patients studied with over 1100 patients now out to 5 years in pooled analysis**
- **Low 7% TLR at 5 years in more than 1100 patients in ENDEAVOR Pooled Analysis**
- **Despite only 39% of patients on DAPT at 1 year in ENDEAVOR Pooled Analysis:[1]**
  - **Observed reduction in ST[2] to 5 years: Endeavor 0.8% *vs.* BMS 1.7%, *p* = 0.051)**
  - **Extremely low 0.2% VLST[2] for Endeavor DES after 1 year through 5 years**
  - **Significant reduction in CD/MI *vs.* BMS at 5 years (Endeavor 5.2% *vs.* BMS 8.4%, *p* = 0.003)**

[1]ENDEAVOR Pooled Analysis: E I 5-year, E II 5-year, E II CA 5-year, E III 5-year, E IV 3-year, E pK 3-year.
[2]ARC definite/probable stent thrombosis definition used.
p-Values are unadjusted for multiple comparisons.
Dual antiplatelet therapy usage based on case report forms. The optimal duration of DAPT, specifically clopidogrel, is unknown and DES thrombosis may still occur despite continued therapy.

Endeavor DES Demonstrated a Significant TLR Reduction in Pooled Analysis

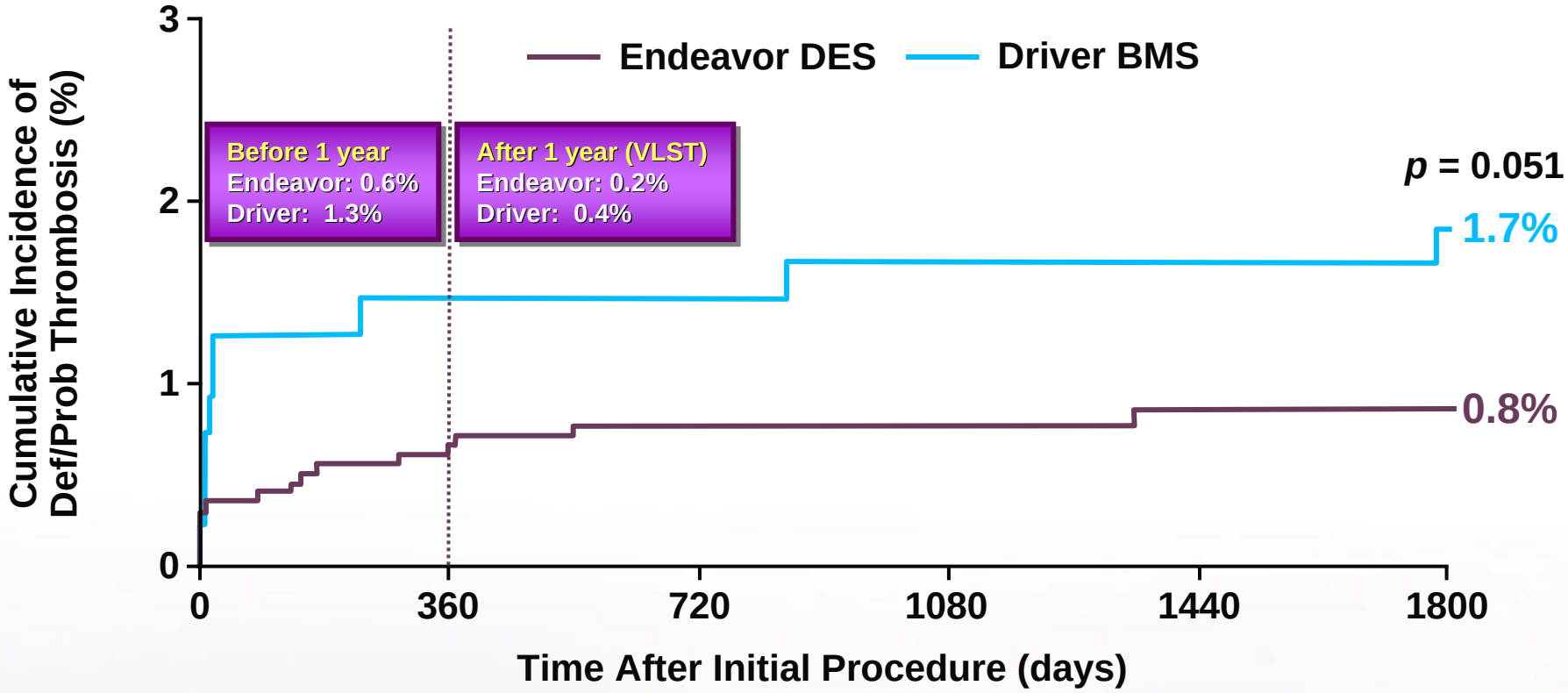


Endeavor	2132	2130	1908	1842	1552	1100
CI (%)	*0.09*	*5.43*	*6.23*	*6.75*	*6.83*	*7.00*
Driver	596	595	489	474	456	445
CI (%)	*0.17*	*13.16*	*14.23*	*14.78*	*15.91*	*16.49*

p-Values are unadjusted for multiple comparisons.
p-Values were calculated by logrank test.
ENDEAVOR Pooled Analysis: E I 5-year, E II 5-year, E II CA 5-year, E III 5-year, E IV 3-year, E pK 3-year.

Observed Reduction in ST vs. BMS at 5 Years in Pooled Analysis

0.2% ARC definite/probable VLST in more than 1100 patients to 5 years

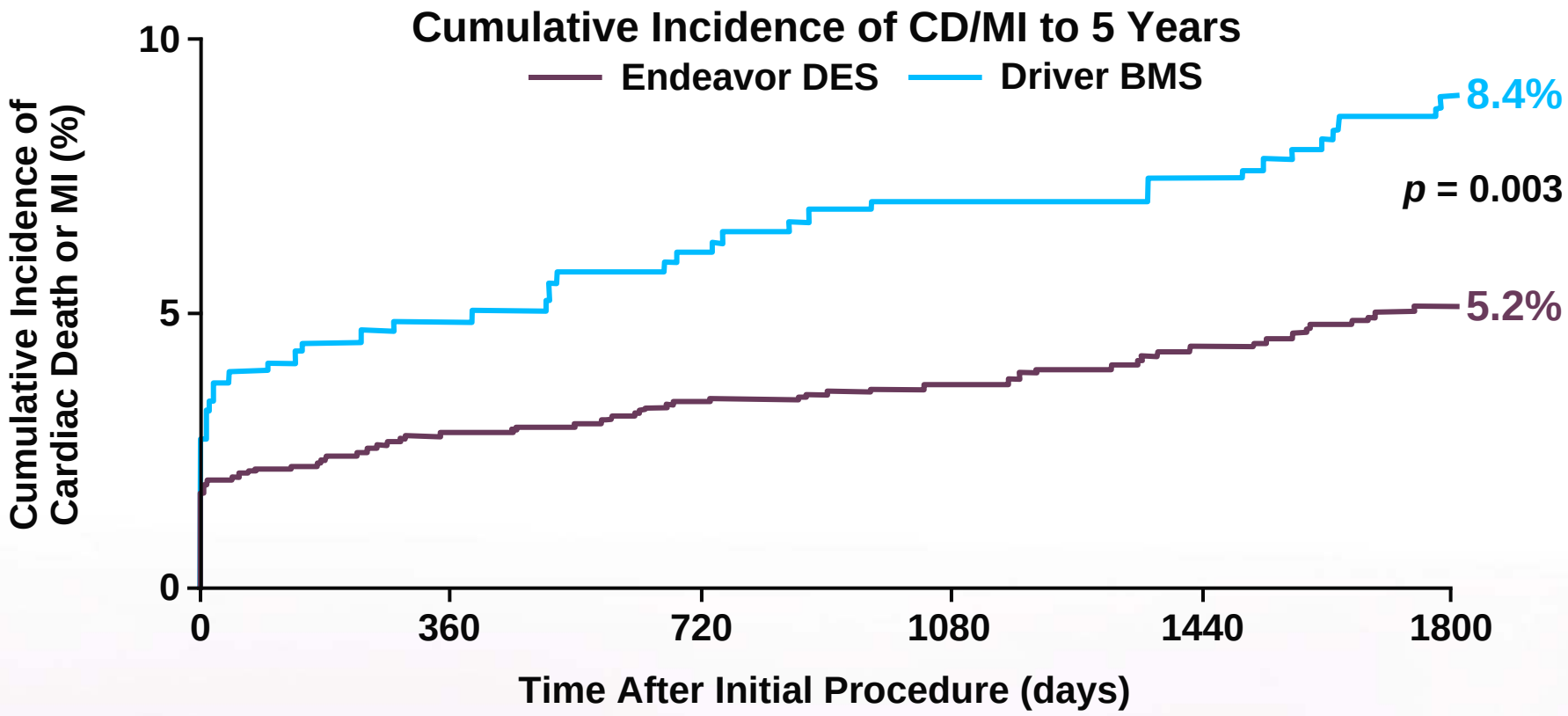


Endeavor	2132	2131	2044	1989	1687	1199
CI (%)	*0.05*	*0.62*	*0.71*	*0.71*	*0.80*	*0.80*
Driver	596	595	570	559	543	538
CI (%)	*0.17*	*1.35*	*1.35*	*1.52*	*1.52*	*1.71*

ENDEAVOR Pooled Analysis: E I 5-year, E II 5-year, E II CA 5-year, E III 5-year, E IV 3-year, E pK 3-year.
By intention to treat (ITT), an Endeavor patient in E III had an ST at 1349 days. Per ARC definition, this uncensored event is included in the primary ITT analysis, although the event may not have been related to the Endeavor stent.

p-Values are unadjusted for multiple comparisons.
p-Values were calculated by logrank test.

Significant Reduction in CD/MI *vs.* BMS at 5 Years in Pooled Analysis



Endeavor	2132	2102	2009	1951	1649	1168
CI (%)	*1.41*	*2.83*	*3.42*	*3.77*	*4.42*	*5.17*
Driver	596	581	555	544	529	523
CI (%)	*2.52*	*4.54*	*5.75*	*6.62*	*6.98*	*8.42*

p-Values are unadjusted for multiple comparisons.
p-Values were calculated by logrank test.
ENDEAVOR Pooled Analysis: E I 5-year, E II 5-year, E II CA 5-year, E III 5-year, E IV 3-year, E pK 3-year.

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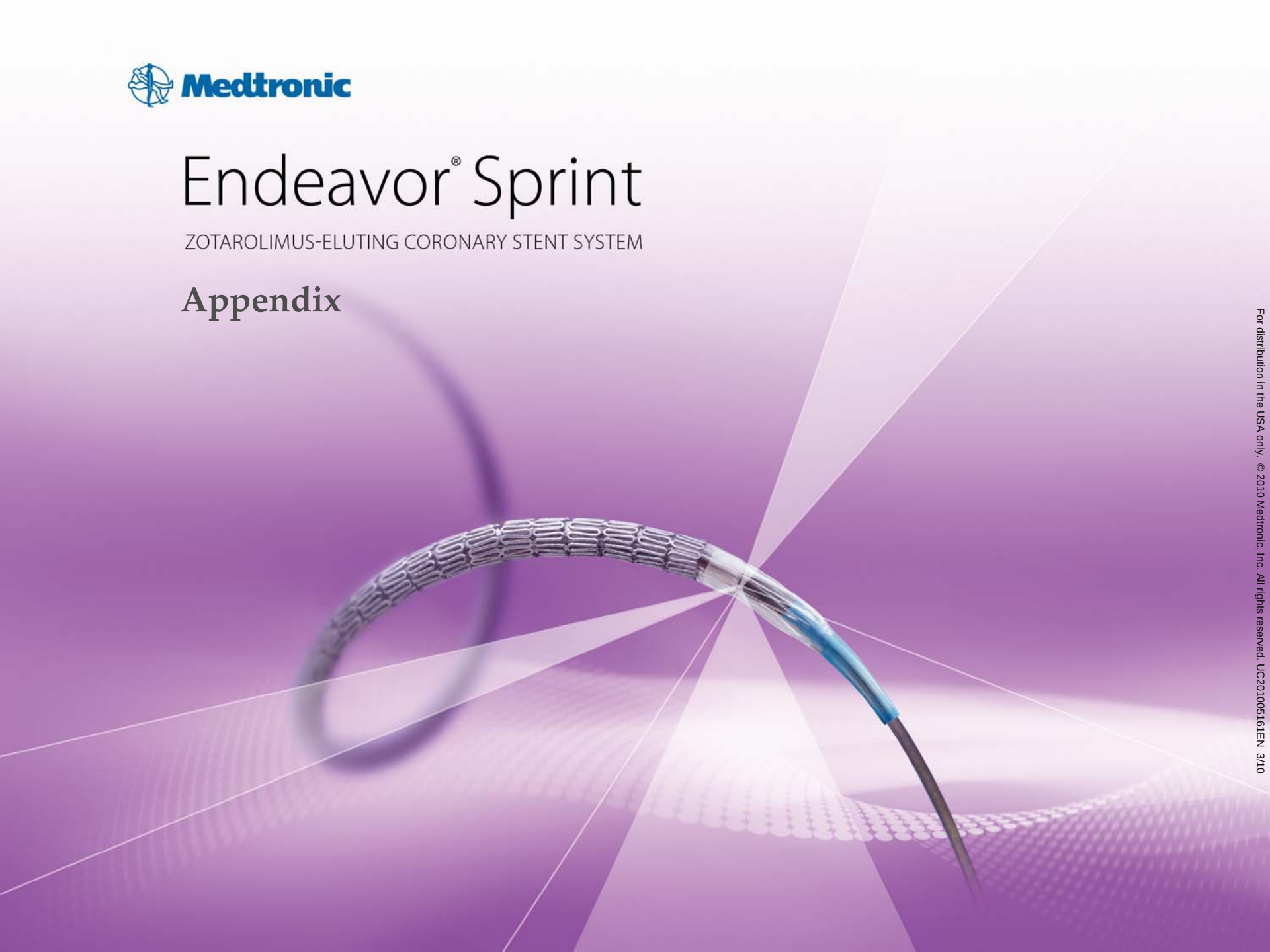
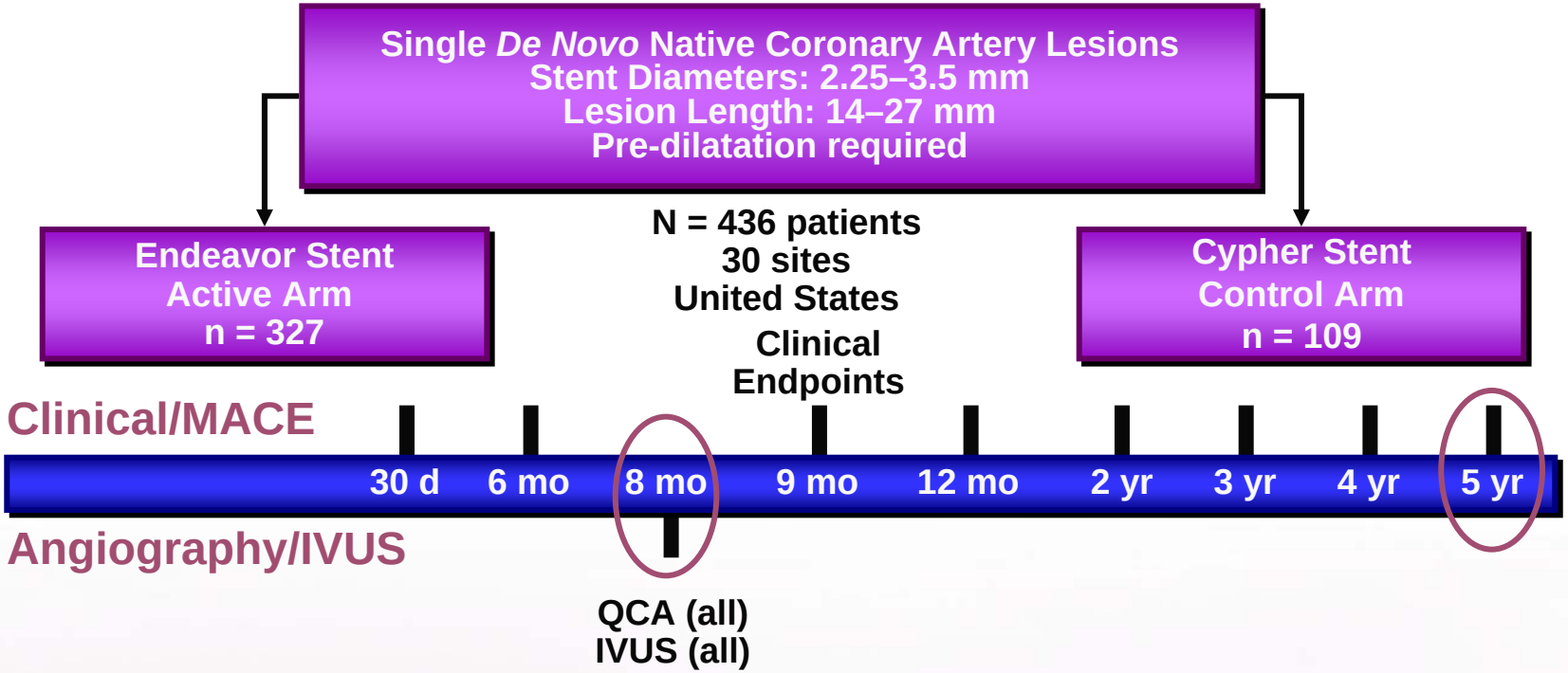
Appendix



ENDEAVOR III

Randomized, controlled trial design; PI Dr. M. Leon



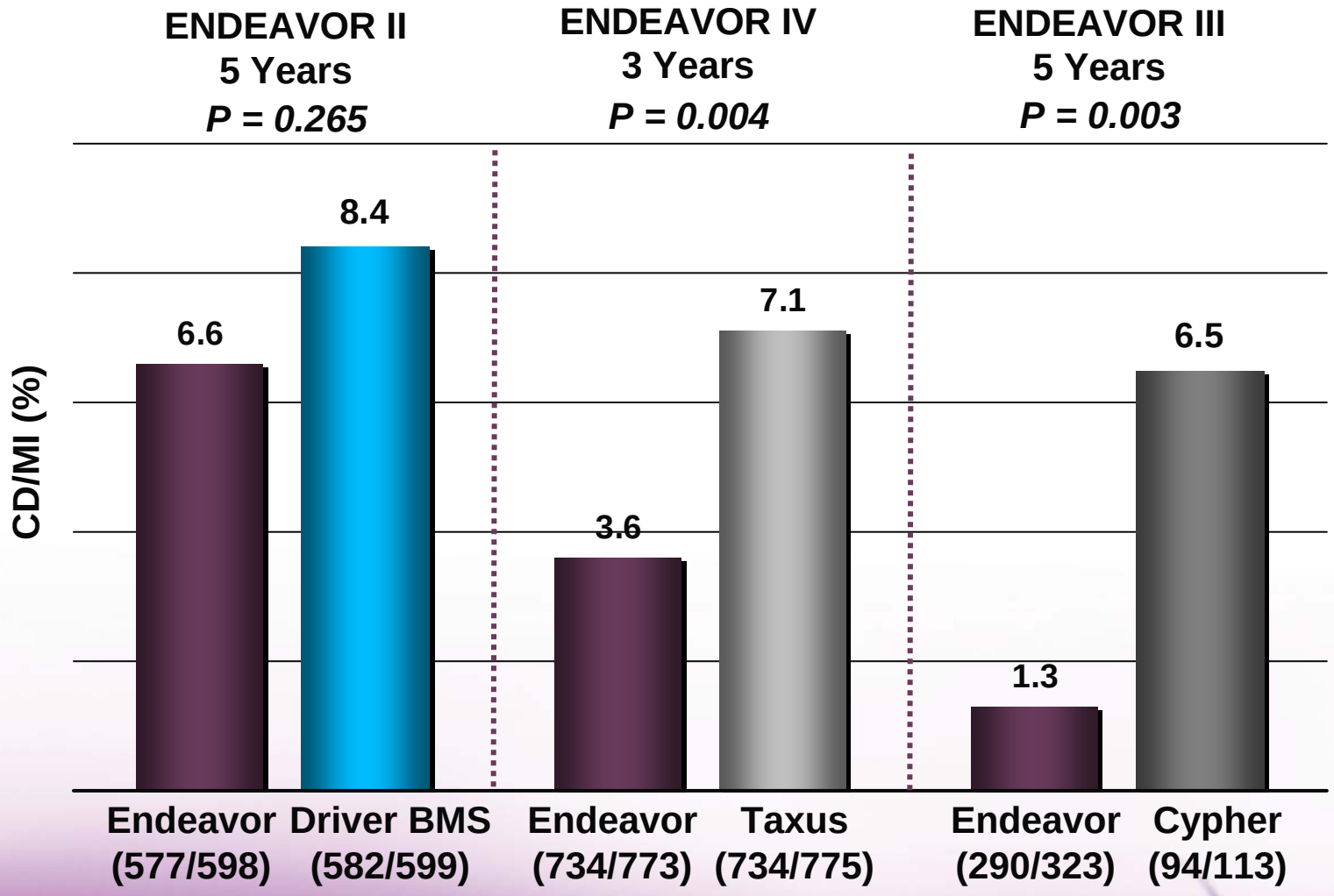
Primary Endpoint: In-segment late lumen loss by QCA at 8 months

Secondary Endpoints: TLR, TVR, TVF at 9 months and ABR at 8 months

Drug Therapy: ASA and Clopidogrel/Ticlid ≥ 3 months

100% angiographic follow-up

Significant Reductions in CD/MI *vs.* Taxus® and Cypher DES



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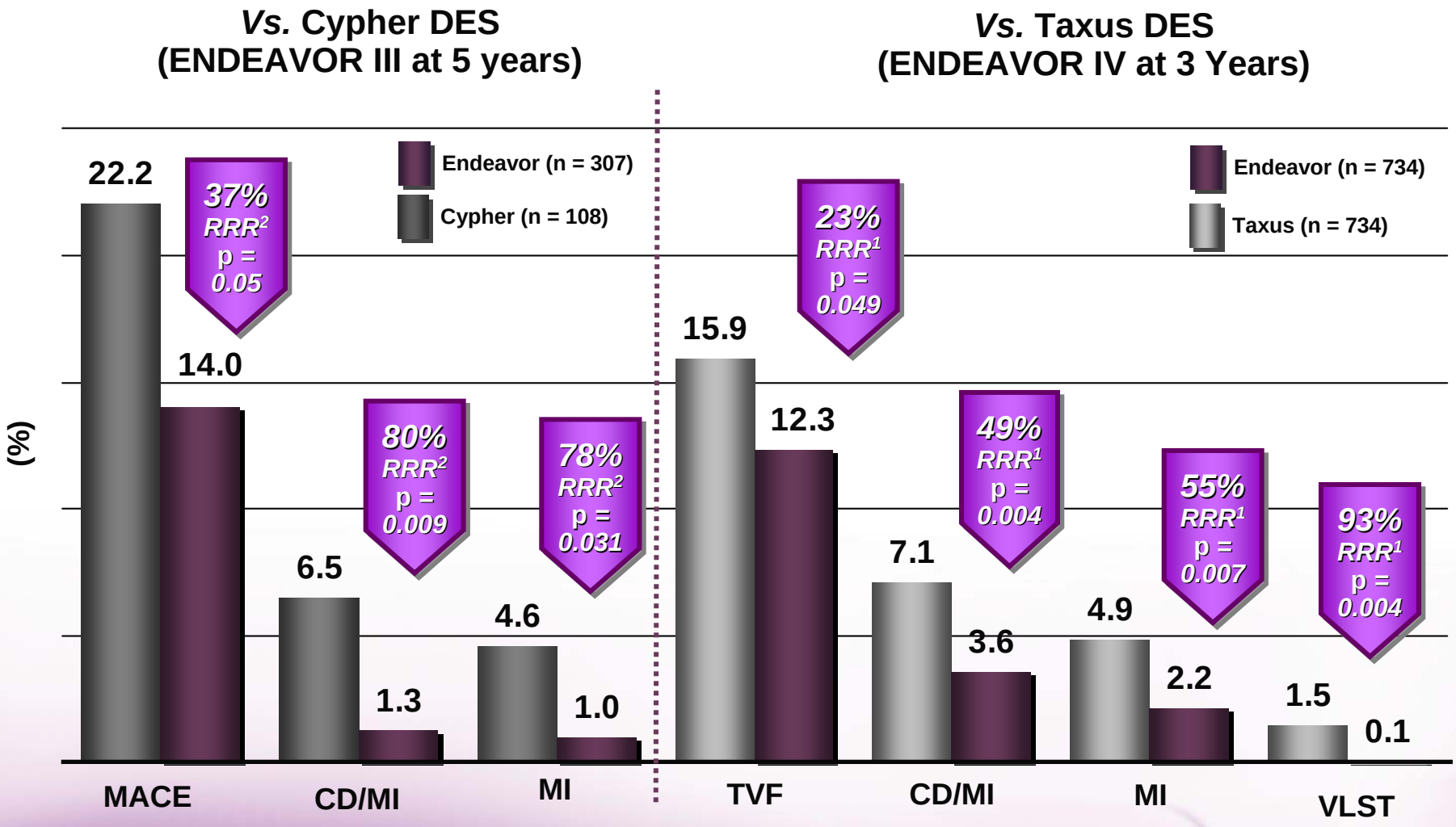
ENDEAVOR II,III, IV *p*-value were calculated by logrank test.
p-values for outcome differences are unadjusted for multiple comparisons.
ENDEAVOR II, III, IV were not specifically designed or powered to individually compare CD/MI.

Endeavor DES Showed Statistically Significant Reductions in Event Rates *vs.* Cypher AND Taxus DES



p-Values for outcome differences are unadjusted for multiple comparisons.
[1]*p*-Values were calculated by logrank test.
[2]*p*-Values were calculated by Fisher's exact test.
ENDEAVOR III was not specifically designed or powered to individually compare MACE, CD/MI or MI.
ENDEAVOR IV was not specifically designed or powered to individually compare TLR, MI, CD/MI or VLST.

Endeavor Sprint ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM

Indications

The Endeavor® Sprint Zotarolimus-Eluting Coronary Stent Delivery System is indicated for improving coronary luminal diameter in patients with ischemic heart disease due to *de novo* lesions of length ≤27 mm in native coronary arteries with reference vessel diameters of ≥2.5 mm to ≤3.5 mm.

Contraindications

The Endeavor Zotarolimus-Eluting Coronary Stent System is contraindicated for use in:

• Patients with a known hypersensitivity to zotarolimus or structurallyrelated compounds • Patients with a known hypersensitivity to the cobalt-based alloy (cobalt, nickel, chromium, and molybdenum) • Patients with a known hypersensitivity to Phosphorylcholine polymer or its individual components.

Coronary artery stenting is contraindicated for use in:

• Patients with a known hypersensitivity or allergies to aspirin, heparin, clopidogrel or ticlopidine • Patients who cannot receive recommended antiplatelet and/or anticoagulation therapy • 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 indicates the sterile barrier has been breached • The use of this product carries the risks associated with coronary artery stenting, including subacute 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 • Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed • Subsequent stent blockage may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized stents is not well characterized • Risks and benefits of the stent should be assessed for patients with history of severe reaction to contrast agents • Do not expose or wipe the product with organic solvents such as alcohol or detergents • Stent thrombosis is a low-frequency event that current drug-eluting stent (DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with myocardial infarction (MI) or death. Data from the ENDEAVOR randomized clinical trials have been prospectively evaluated and adjudicated using both the protocol definition of stent thrombosis and the definition developed by the Academic Research Consortium (ARC), and demonstrate specific patterns of stent thrombosis that vary depending on the definition used. In the ENDEAVOR clinical trials analyzed to date, the differences in the incidence of stent thrombosis observed with the Endeavor stent compared to bare metal stents have not been associated with an increased risk of cardiac death, MI, or all cause mortality. Additional data from longer-term follow-up in the ENDEAVOR randomized clinical trials and analyses of DES-related stent thrombosis are expected and should be considered in making treatment decisions as data become available • When DES are used outside the specified *Indications for Use*, patient outcomes may differ from the results observed in the pivotal clinical trials • Compared to use within the specified *Indications for Use,* the use of DES in patients and lesions outside of the labeled indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death.

The safety and effectiveness of the Endeavor stent have not yet been established in the following patient populations:

• Women who are pregnant or lactating • Men intending to father children • Pediatric patients • Patients with vessel thrombus at the lesion site • Patients with coronary artery reference vessel diameters <2.5 mm or >3.5 mm • Patients with coronary artery lesions longer than 27 mm or requiring more than one Endeavor stent • Patients with lesions located in saphenous vein grafts, in the unprotected left main coronary artery, ostial lesions, or lesions located at a bifurcation • Patients with diffuse disease or poor flow distal to the identified lesions • Patients with multivessel disease • Patients with tortuous vessels in the region of the obstruction or proximal to the lesion • Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow • Patients for longer than 48 months of follow-up • Patients with in-stent restenosis • Patients with moderate or severe calcification in the lesion or a chronic total occlusion • Patients with prior brachytherapy of the target lesion or the use of brachytherapy to treat in-stent restenosis in an Endeavor stent.

The safety and effectiveness of the Endeavor 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 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 • Balloon rupture • 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 • Late or very late thrombosis • Myocardial infarction (MI) • Myocardial ischemia • Peripheral ischemia/peripheral nerve injury • Renal failure • Restenosis of the stented artery • Rupture of native or bypass graft • Shock/pulmonary edema • Stent deformation, collapse, or fracture • Stent migration • Stent misplacement • Stroke/transient ischemic attack • Thrombosis (acute and subacute) • Unstable angina • Ventricular fibrillation.

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 • Anemia • Application site reaction • 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.

Medtronic Vascular
3576 Unocal Place
Santa Rosa, CA 95403
USA
Tel: 707.525.0111

www.Medtronic.com
www.EndeavorStent.com

CardioVascular LifeLine
Customer Support
Tel: 877.526.7890
Tel: 763.526.7890

Product Services
Tel: 888.283.7868
Fax: 800.838.3103

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