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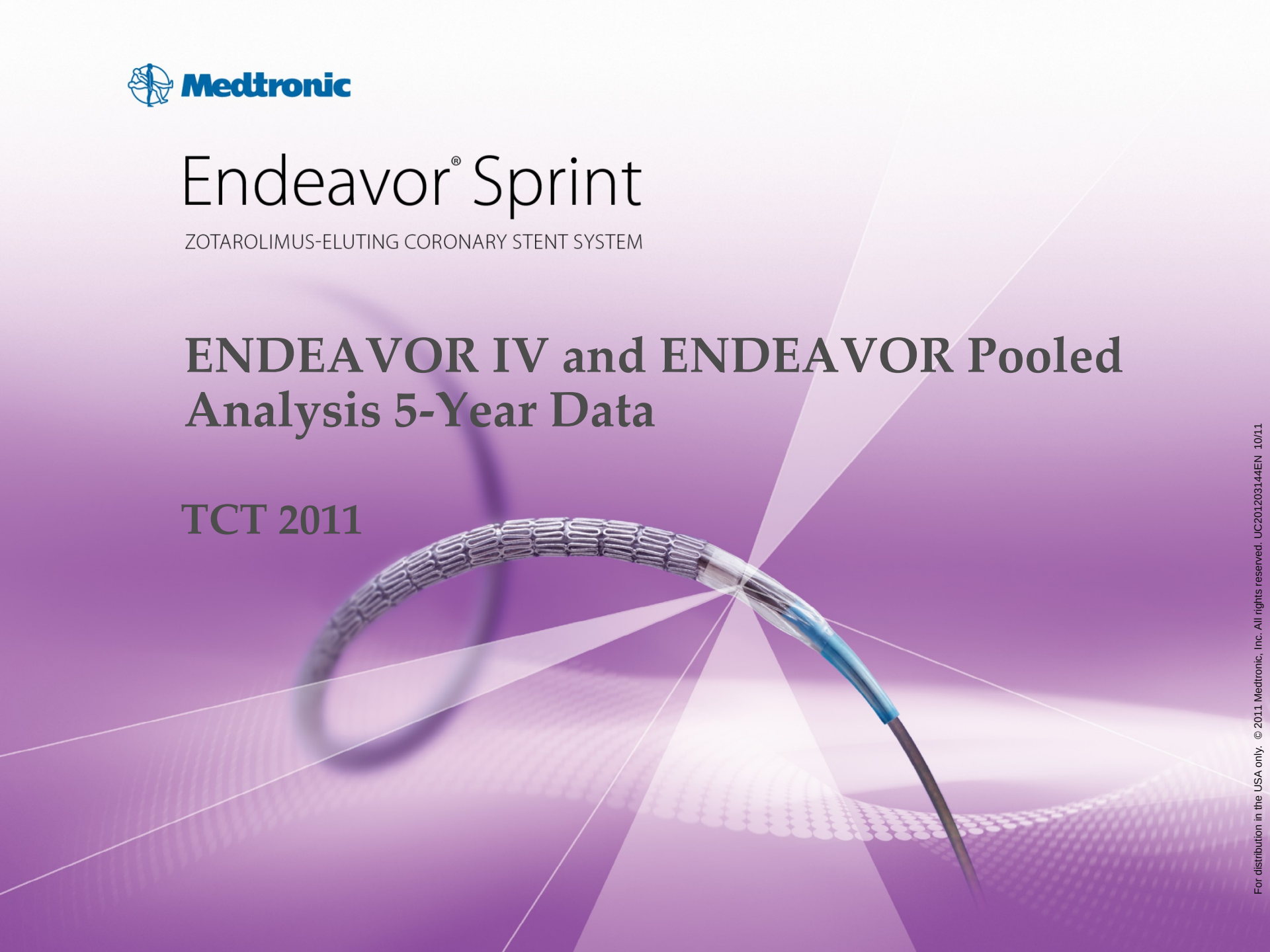
Endeavor® Sprint

ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM

ENDEAVOR IV and ENDEAVOR Pooled Analysis 5-Year Data

TCT 2011



ENDEAVOR IV and ENDEAVOR Pooled Results at 5 Years

ENDEAVOR IV

- **Statistically significant difference in safety event rates for Endeavor DES vs. Taxus® DES**
  - 78% significant relative risk reduction in ARC definite/probable VLST ($p = 0.012$)
  - 30% significant relative risk reduction in CD/MI ($p = 0.048$)
- **TLR catch-up with Taxus DES leads to similar TLR**
  - 161% Increase with Taxus DES vs. only 71% TLR Increase with Endeavor DES from 1 to 5 years

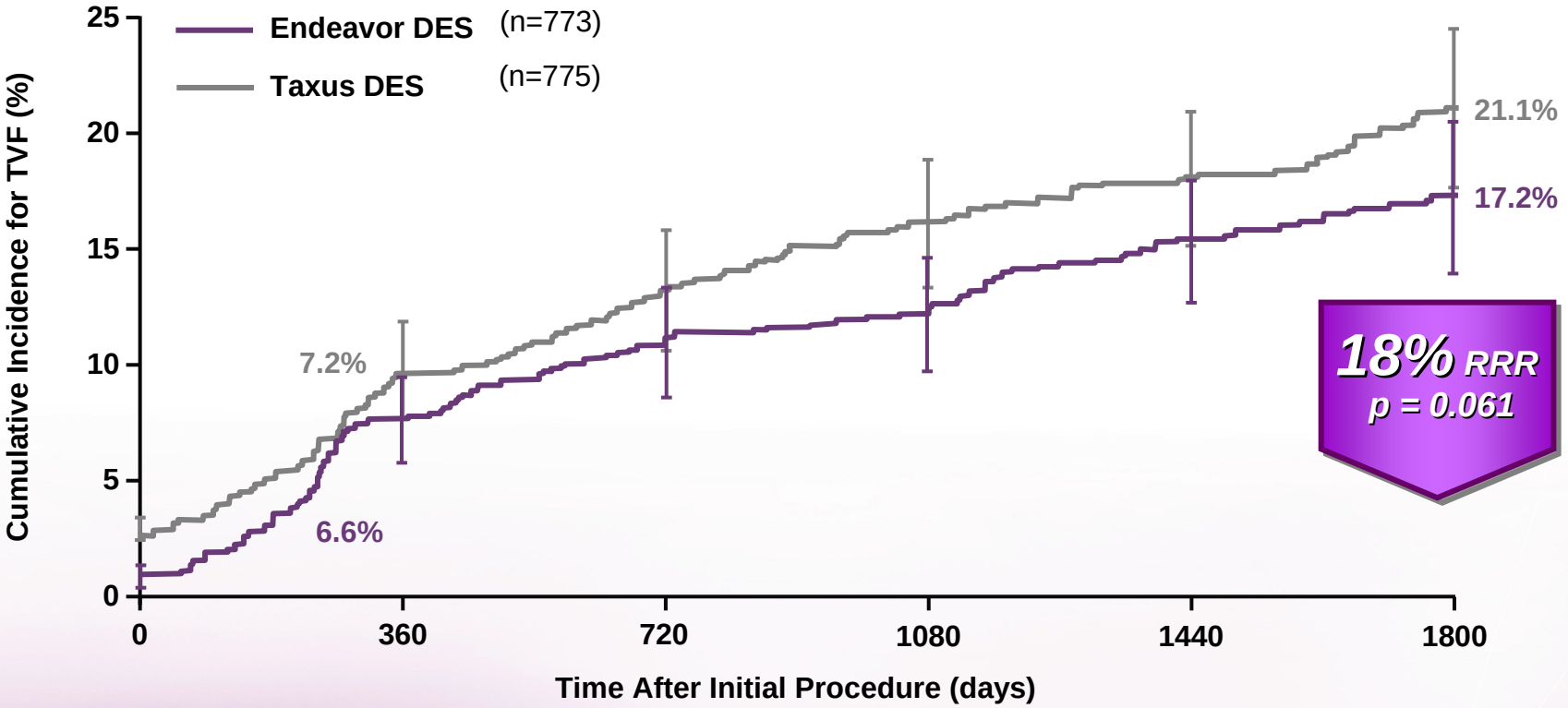
ENDEAVOR Pooled

- **Low ENDEAVOR Pooled composite and component event rates**

p-Values were calculated by logrank test.
ENDEAVOR IV primary endpoint: noninferiority of Endeavor DES to Taxus DES at 9 months (target vessel failure).
ENDEAVOR IV was not specifically designed or powered to individually compare TLR, CD/MI or VLST.
p-Values for outcome differences are unadjusted for multiple comparisons.

18% Observed Relative Risk Reduction in TVF

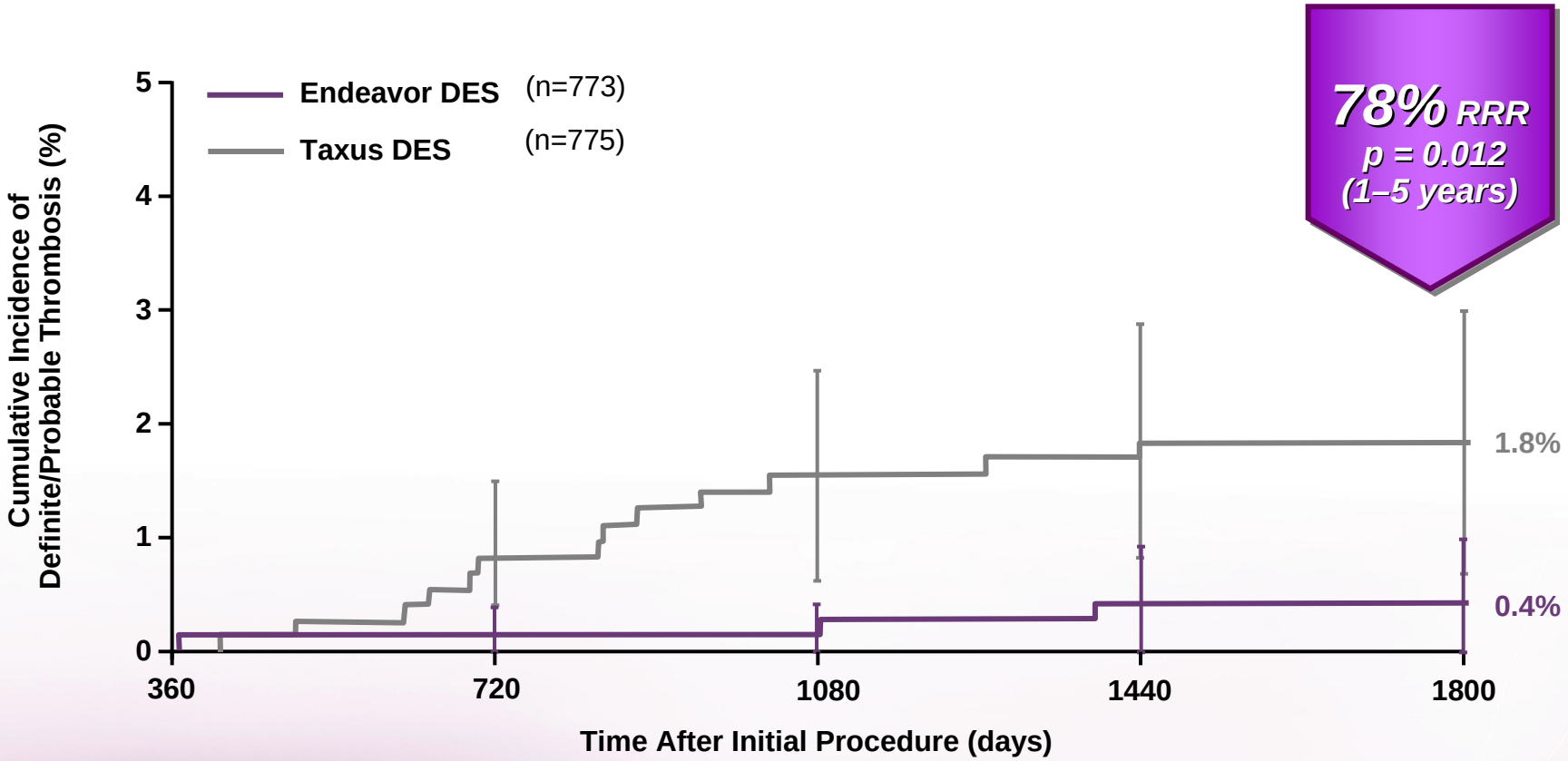
ENDEAVOR IV at 5 Years



p-Values were calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons.
ENDEAVOR IV primary endpoint: noninferiority of Endeavor DES to Taxus DES at 9 months (target vessel failure).
RRR = relative risk reduction

78% Significant Relative Risk Reduction in Very Late Stent Thrombosis

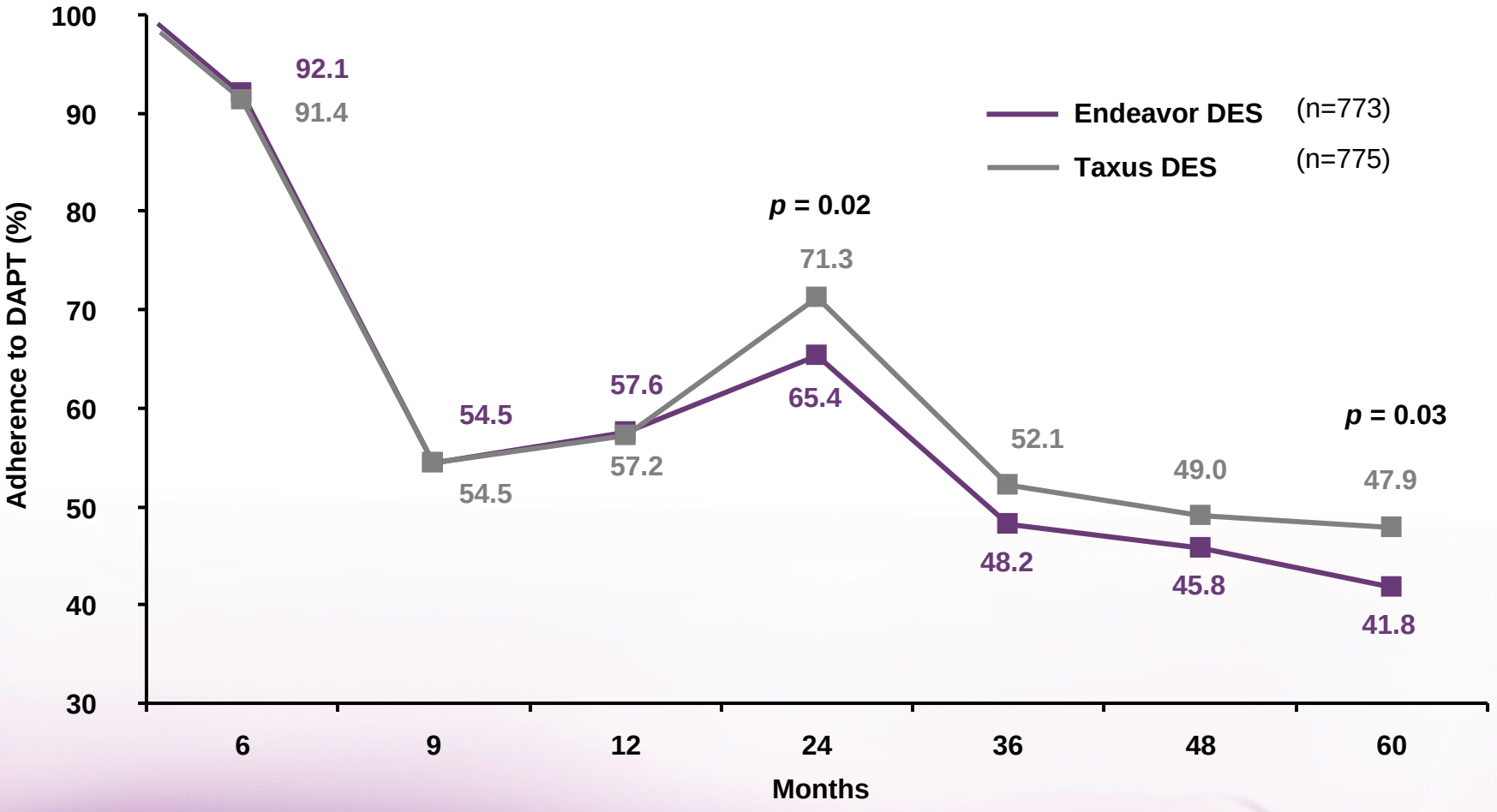
ENDEAVOR IV at 5 Years: ARC Definite/Probable ST



p-Values were calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons.
ENDEAVOR IV was not specifically designed or powered to individually compare VLST.
RRR = relative risk reduction

ENDEAVOR IV

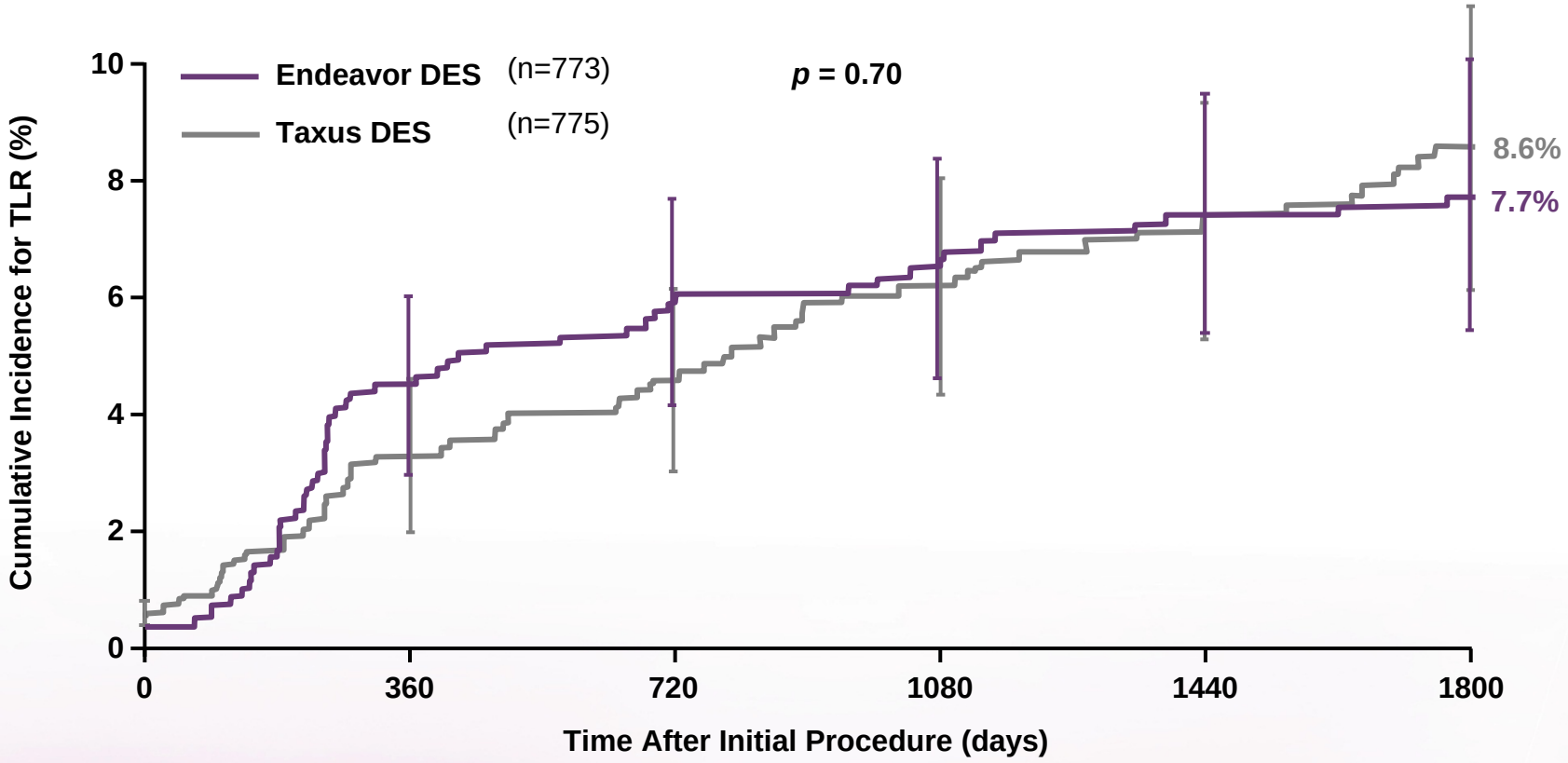
Dual Antiplatelet Therapy Use to 5 Years



The optimal duration of dual antiplatelet therapy, specifically clopidogrel, is unknown and DES thrombosis may still occur despite continued therapy.
DAPT usage based on case report forms and reported at the time points shown.
Trend line is for illustrative purposes only and does not represent continuous reporting.

Late Catch up with Taxus DES

ENDEAVOR IV shows similar TLR rates at 5 years

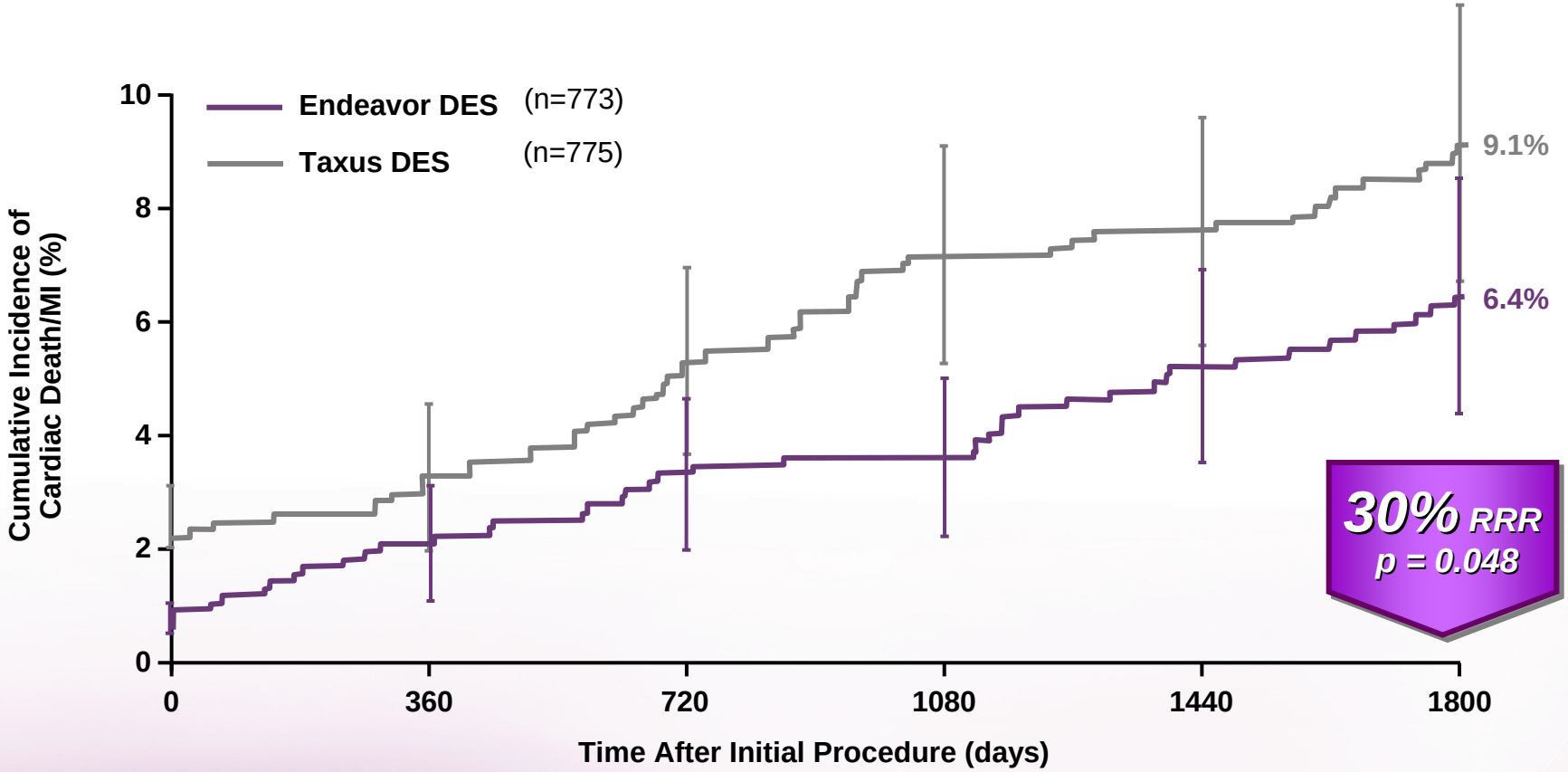


161% Increase with Taxus DES vs. only 71% TLR Increase with Endeavor DES from 1 to 5 years

p-Value was calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons. ENDEAVOR IV was not specifically designed or powered to individually compare TLR.

30% Significant Relative Risk Reduction in Cardiac Death/MI

ENDEAVOR IV at 5 Years



p-Values were calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons.
ENDEAVOR IV was not specifically designed or powered to individually compare CD/MI.
RRR = relative risk reduction

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ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM

Taxus DES vs ION DES

Same Drug, Same Polymer, Same Potential Results

ION DES: New Platform, Same Drug and Polymer

It's Still a Taxus Stent

		Taxus Liberté® DES	ION (Taxus Element) DES
Same	Drug	Paclitaxel	
Same	Polymer	SIBS (hydrophobic)	
Same	Drug elution profile	90% of the drug never elutes	
Different	Platform	Liberté	Element
Different	Platform material	Stainless steel	Platinum chromium
Different	Delivery system	Maverick 2	ION delivery system

Taxus Liberté DES

ION (Taxus Element) DES

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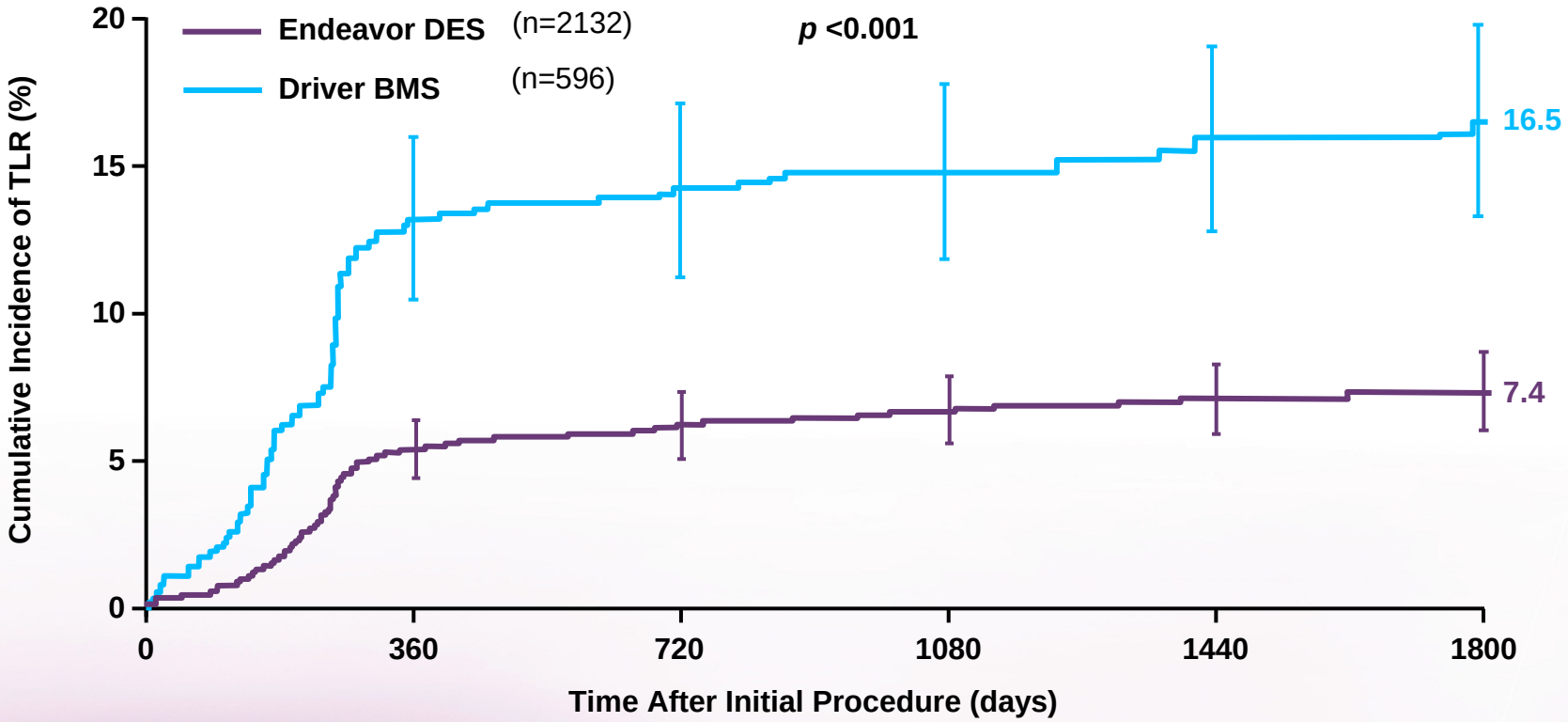
ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM

ENDEAVOR Pooled Is Consistent with ENDEAVOR IV

Endeavor Demonstrates a Significant TLR Reduction in Pooled Analysis

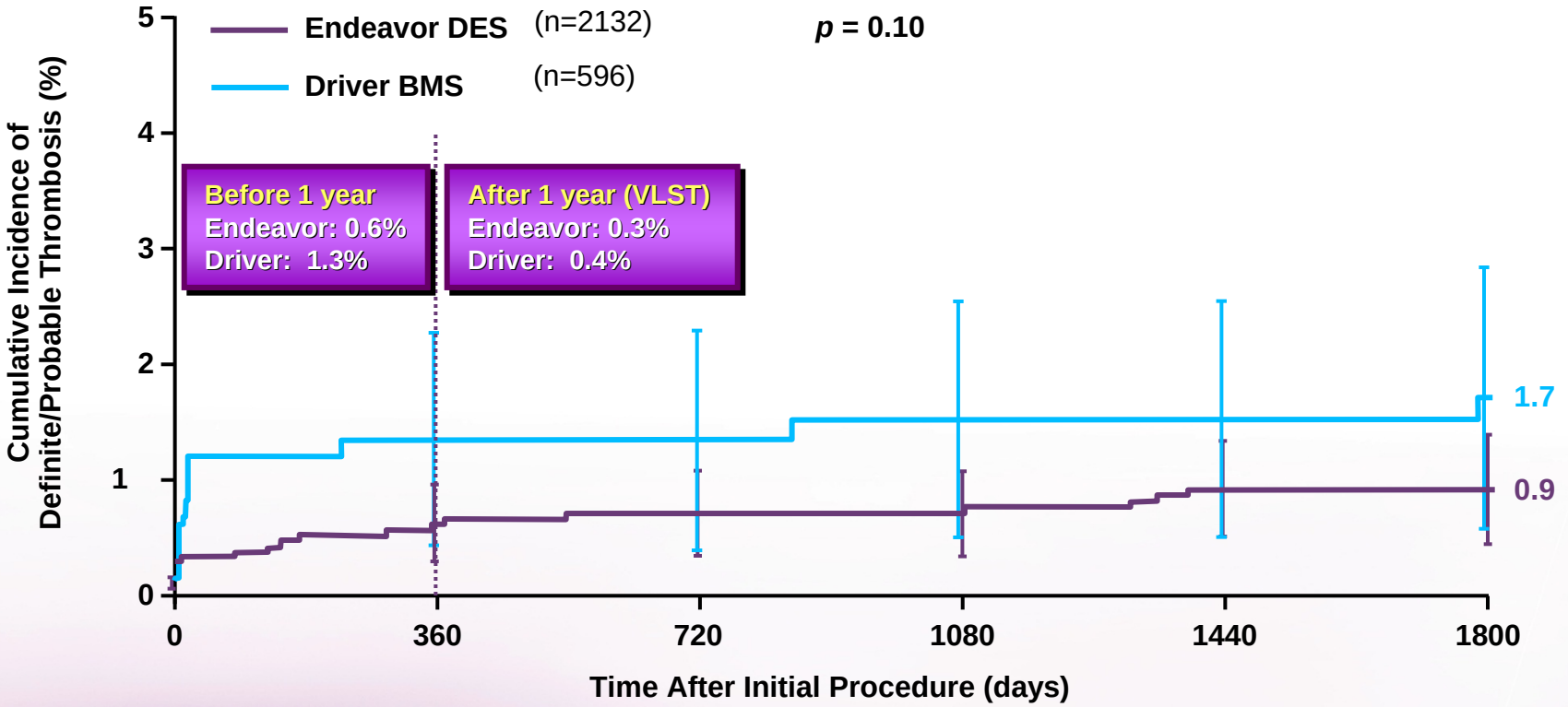
ENDEAVOR Pooled vs. Driver BMS at 5 Years



Pooled data used for analysis: E I 5-yr, E II 5-yr, E II CA 5-yr, E III 5-yr, E IV 5-yr, E pK 5-yr.
Driver data came from ENDEAVOR II.
Values were calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons.

0.3% ARC definite/probable VLST in more than 1000 patients to 5 years

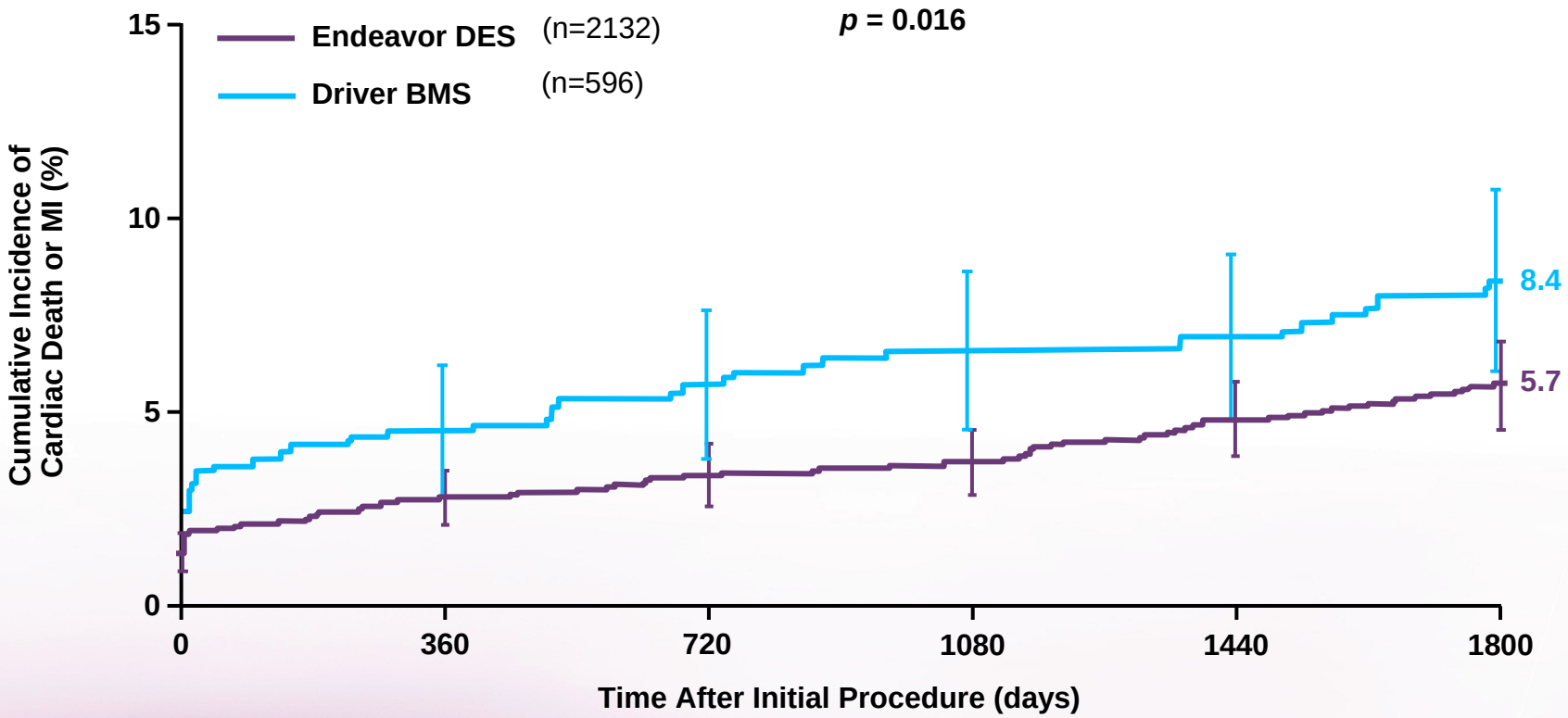
ENDEAVOR Pooled vs. Driver BMS: ARC Definite/Probable ST at 5 Years



Pooled data used for analysis: E I 5-yr, E II 5-yr, E II CA 5-yr, E III 5-yr, E IV 5-yr, E pK 5-yr.
Driver data came from ENDEAVOR II.
Values were calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons.

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

ENDEAVOR Pooled vs. Driver BMS at 5 Years



Pooled data used for analysis: E I 5-yr, E II 5-yr, E II CA 5-yr, E III 5-yr, E IV 5-yr, E pK 5-yr. Driver data came from ENDEAVOR II. *p*-Values were calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons.

ENDEAVOR IV and ENDEAVOR Pooled Results at 5 Years

ENDEAVOR IV

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ENDEAVOR IV primary endpoint: noninferiority of Endeavor DES to Taxus DES at 9 months (target vessel failure).
ENDEAVOR IV was not specifically designed or powered to individually compare TLR, CD/MI or VLST.
p-Values for outcome differences are unadjusted for multiple comparisons.

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 structurally related 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 allcause 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.

www.medtronic.com
www.medtronicstents.com

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Endeavor Sprint ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM

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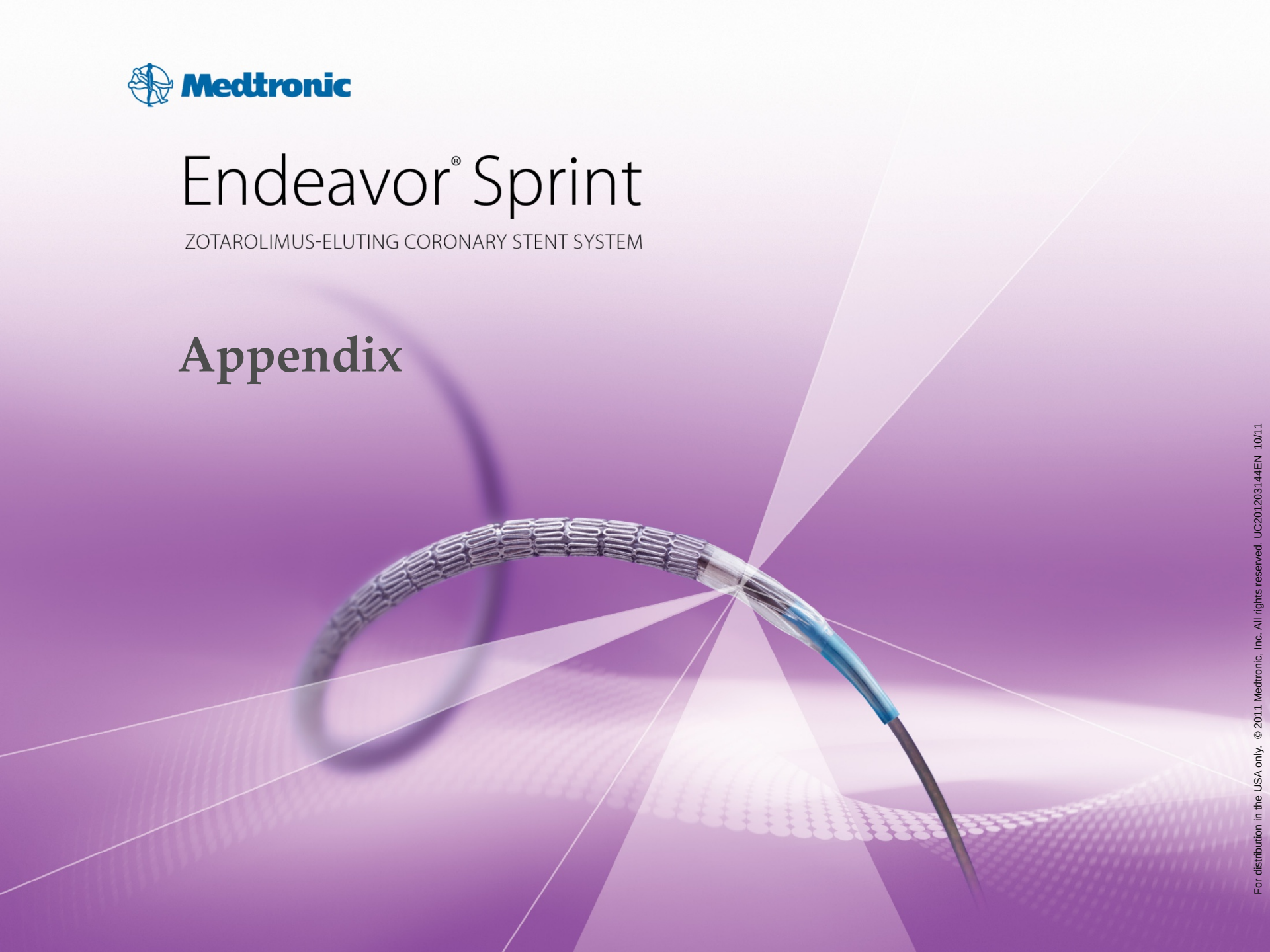
ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM

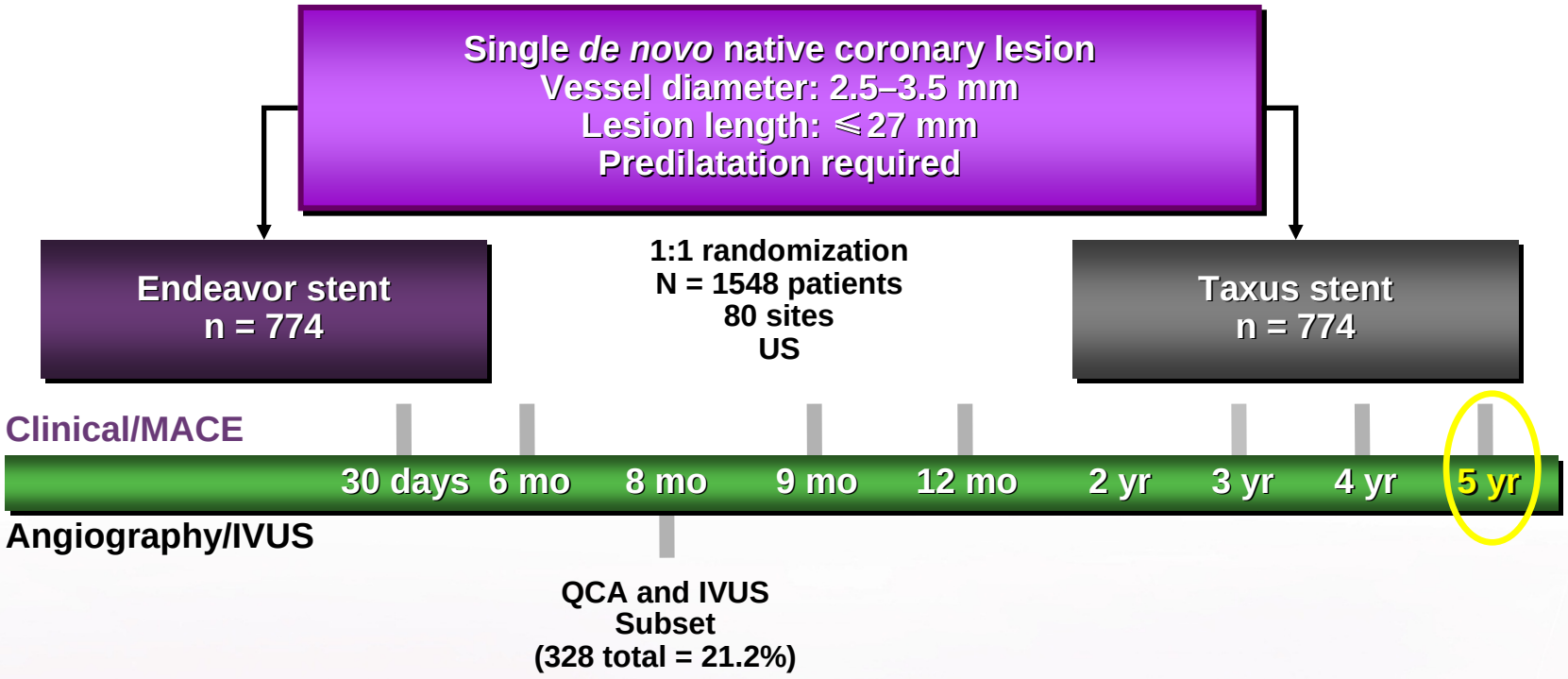
Appendix



ENDEAVOR IV: 5-Year Follow-Up

Clinical Trial Design

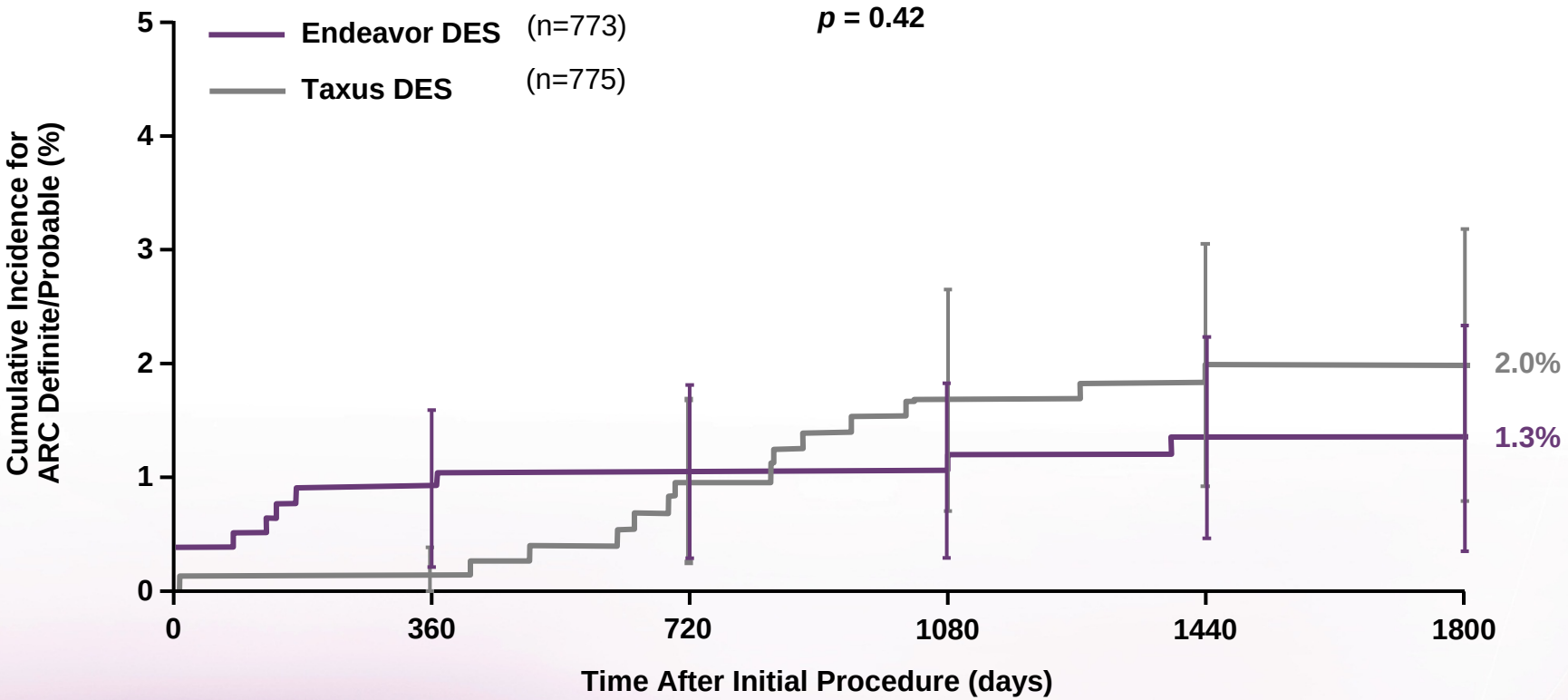
Principal Investigators: Martin B. Leon, MD, and David E. Kandzari, MD



Primary endpoint: TVF at 9 months
Secondary endpoints: In-segment % DS at 8 months
TLR and TVR at 9 months
Drug therapy: ASA and clopidogrel/Ticlid® ≥ 6 months
Zotarolimus dose: 10 µg per mm stent length

ENDEAVOR IV

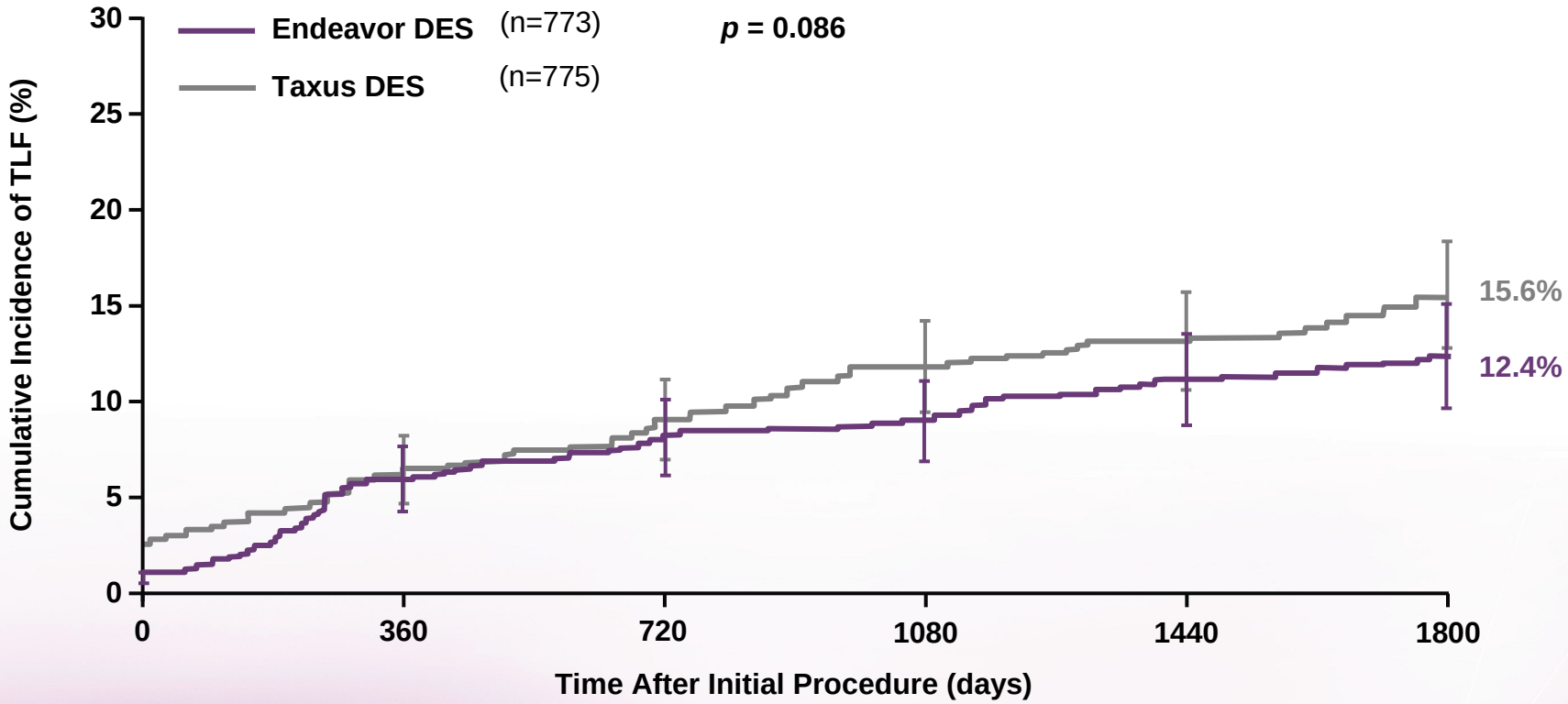
Cumulative Incidence of ARC ST Definite/Probable to 5 Years



p-Values were calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons.
ENDEAVOR IV was not specifically designed or powered to individually compare ST.
RRR = relative risk reduction

ENDEAVOR IV

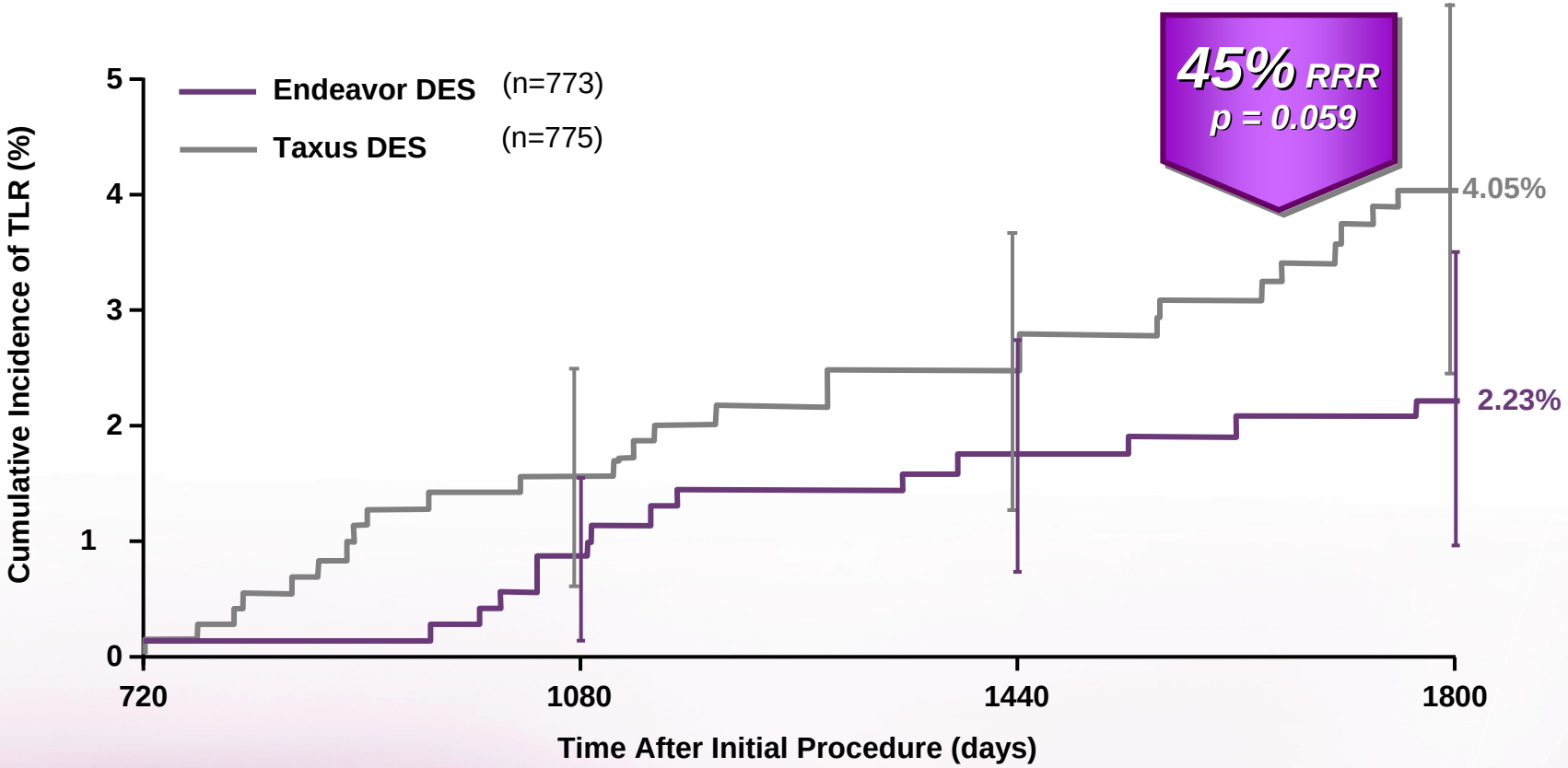
Cumulative Incidence of TLF to 5 Years



p-Value was calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons. ENDEAVOR IV was not specifically designed or powered to individually compare TLF.

45% Observed Relative Risk Reduction at 5 Years in TLR between 2 and 5 Years

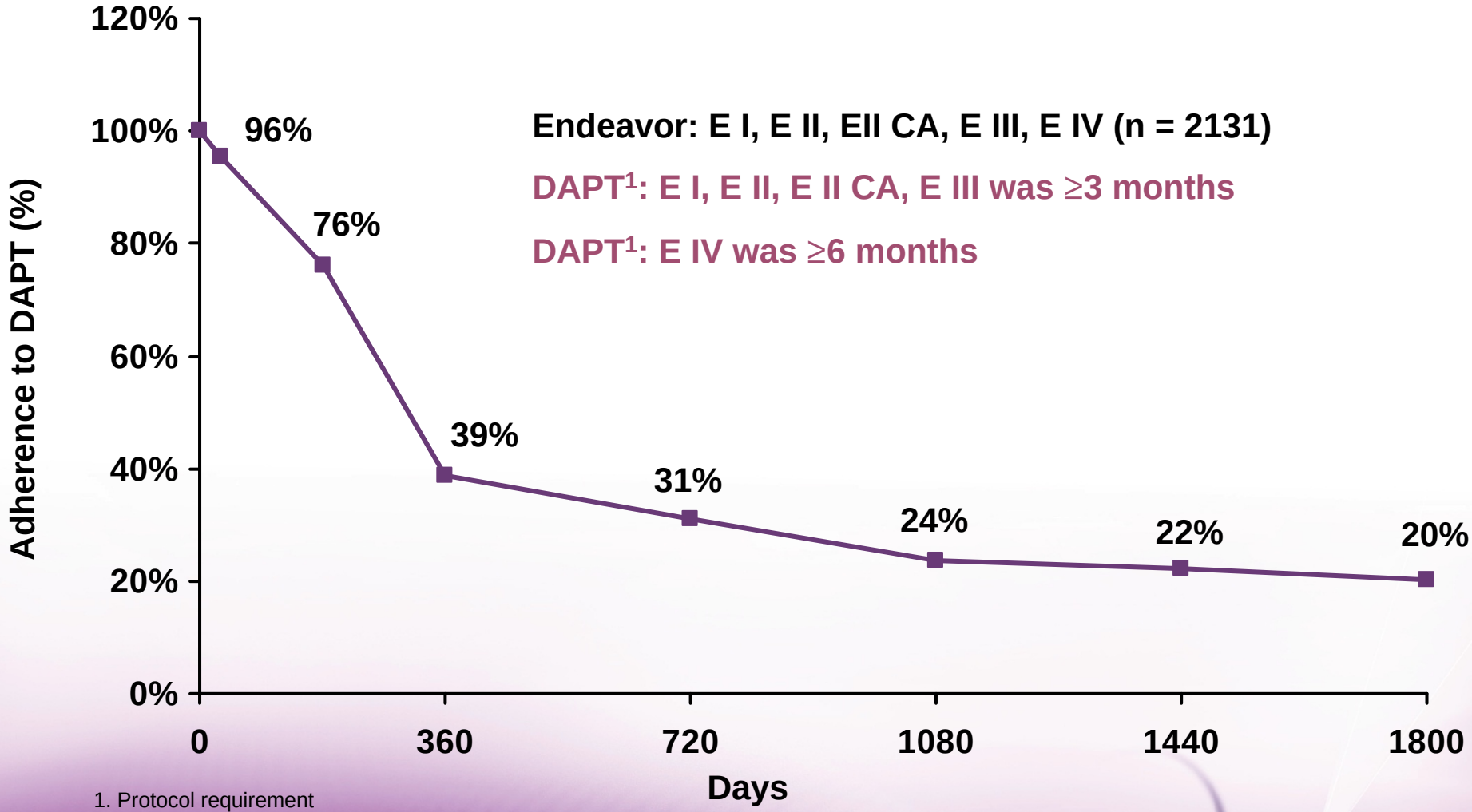
ENDEAVOR IV at 5 Years



p-Value was calculated by logrank test. *p*-Values for outcome differences are unadjusted for multiple comparisons.
ENDEAVOR IV was not specifically designed or powered to individually compare TLR.
RRR = relative risk reduction

Excellent Safety Despite Only 39% of Endeavor Patients on DAPT at 1 Year

ENDEAVOR Pooled DAPT Compliance

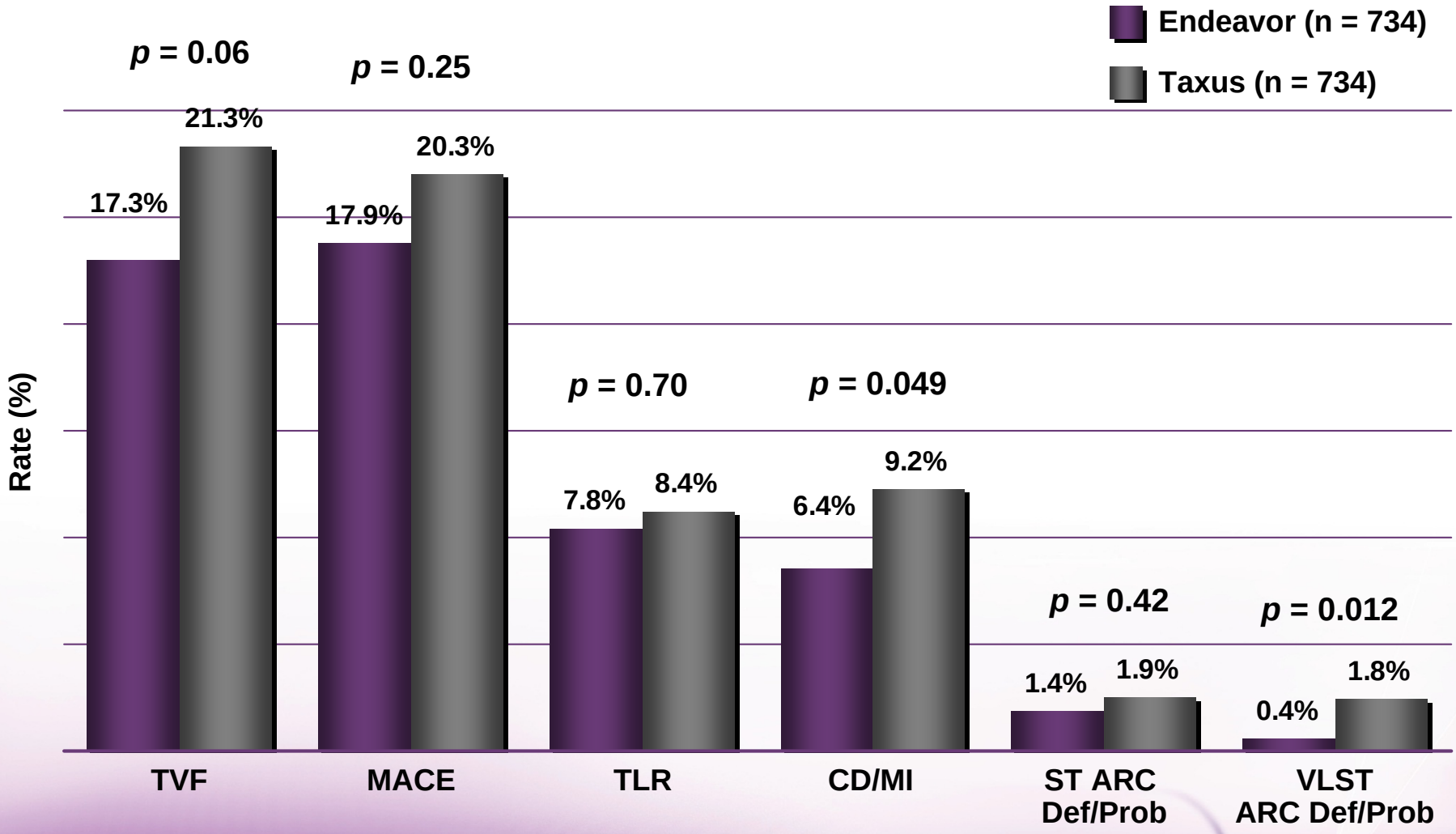


1. Protocol requirement

The optimal duration of dual antiplatelet therapy, specifically clopidogrel, is unknown and DES thrombosis may still occur despite continued therapy. DAPT usage based on case report forms and reported at the time points shown. Trend line is for illustrative purposes only and does not represent continuous reporting.

Clinical Performance at 5 Years

ENDEAVOR IV Endpoints



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