

SORT OUT III

Perspectives on 18-Month Results

SORT OUT III Perspectives

- **Concerns with SORT OUT III Methodology:** The SORT OUT III study uses an unconventional methodology that raises questions regarding the reproducibility and viability of the results
- **Inconsistency of Data for Cypher® DES:** SORT OUT III shows unexpectedly low rates and inconsistent data for Cypher compared with nearly every other trial utilizing the Cypher stent
- **SORT OUT III Results Are Short-Term Only:** The long-term deficiencies of Cypher demonstrated in multiple studies are not addressed by the short-term focus of SORT OUT III
- **Consistency of Data for Endeavor® DES:** While the SORT OUT III data are inconsistent for Cypher, the Endeavor outcomes in SORT OUT III reinforce the low and durable event rates for the Endeavor stent

SORT OUT III

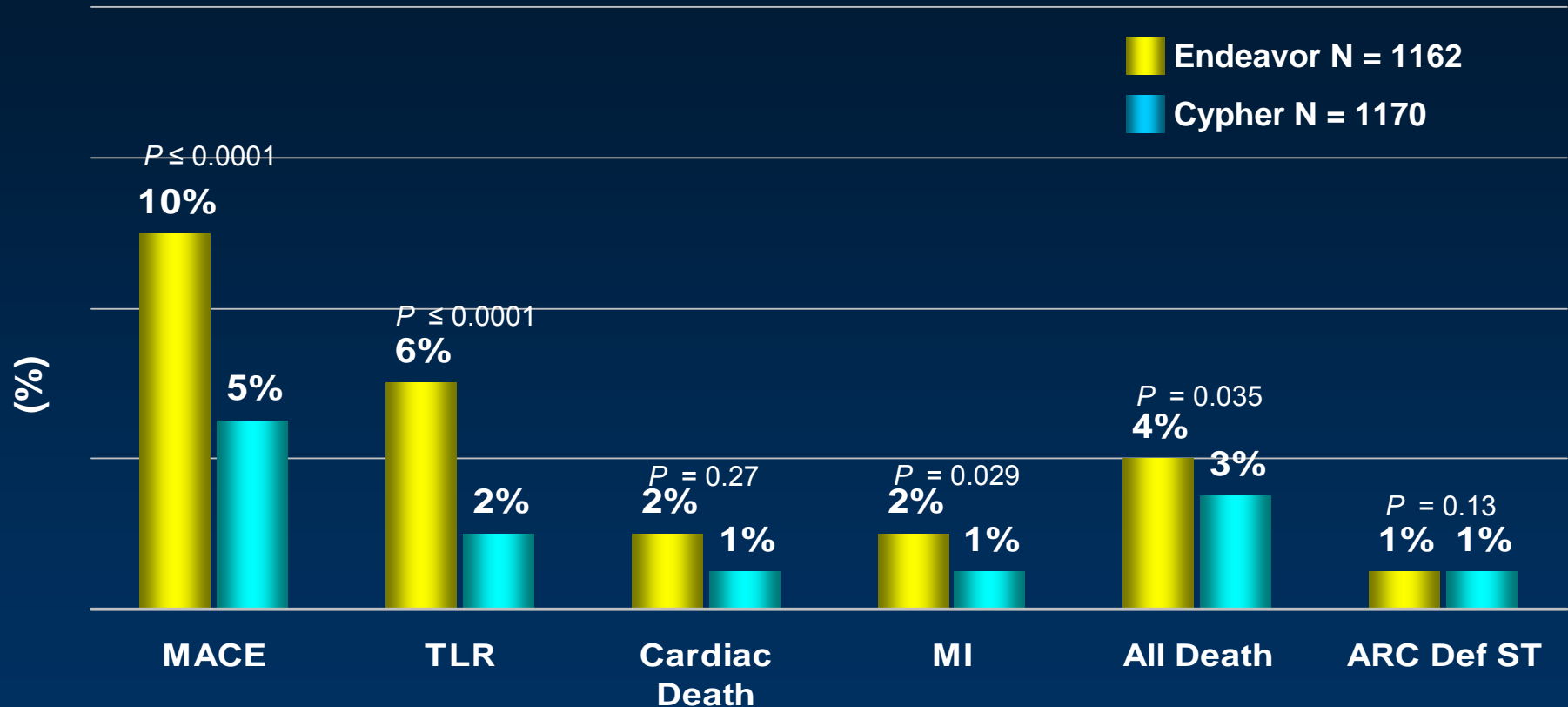
Questionable Trial Methodology

1. Positioned as a randomized “real-world” study yet nearly 60% (3344) of eligible patients were excluded in the analysis
2. Unlike controlled trials with rigorous patient follow-up, SORT OUT III is dependent on patient records from a national database
3. Investigators themselves—not an independent clinical events committee—determined and verified stent thrombosis (ST), target lesion revascularization (TLR), myocardial infarction (MI) and restenosis
4. Procedure-related MIs were not captured, which may introduce bias because other studies utilizing these two stents have demonstrated a high rate of periprocedural MIs with Cypher and a low rate with Endeavor¹
5. Differences in patient adherence to DAPT regimens were not reported despite the potential effect on safety outcomes

¹ In-Hospital MI rates: Cypher 2.3%, BMS 1.5% (SIRIUS Trial); Cypher 3.5%, Endeavor 0.6% (ENDEAVOR III Trial)

SORT OUT III

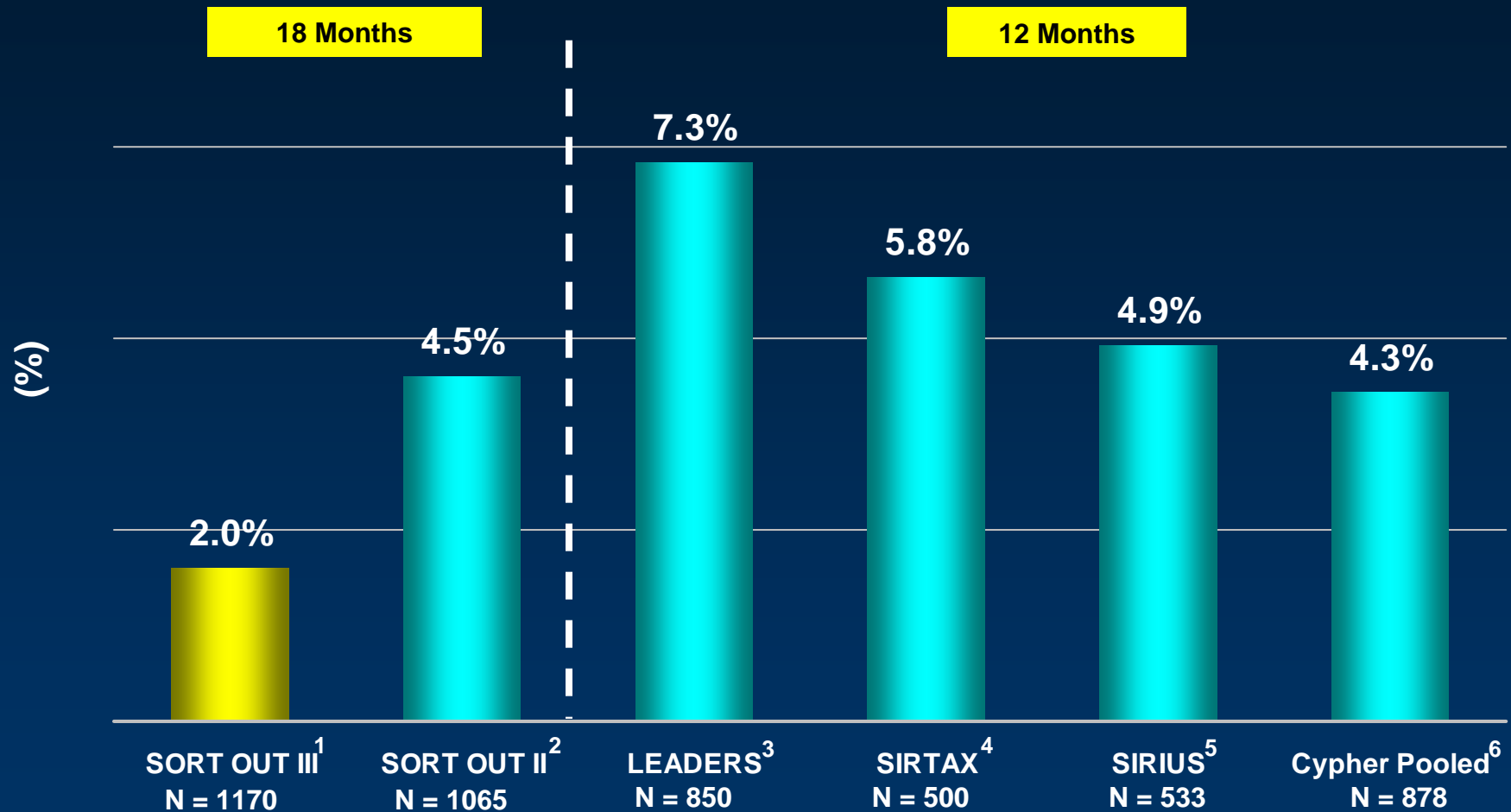
Event Rates at 18 Months



- The MACE and MI rates in SORT OUT III exclude periprocedural MI
- In ENDEAVOR III procedural MI = Cypher 3.5% vs. Endeavor 0.6% ($p = 0.042$); therefore the impact on the MACE and MI rates in SORT OUT III is unknown

Cypher: SORT OUT III TLR

Inconsistent Clinical Evidence



¹ Rasmussen K et al. Lancet, Published Online March 15, 2010

² Galloe AM et al., JAMA, 299:4 pp. 409-416, 2008.

³ Klaus V et al., TCT 2009

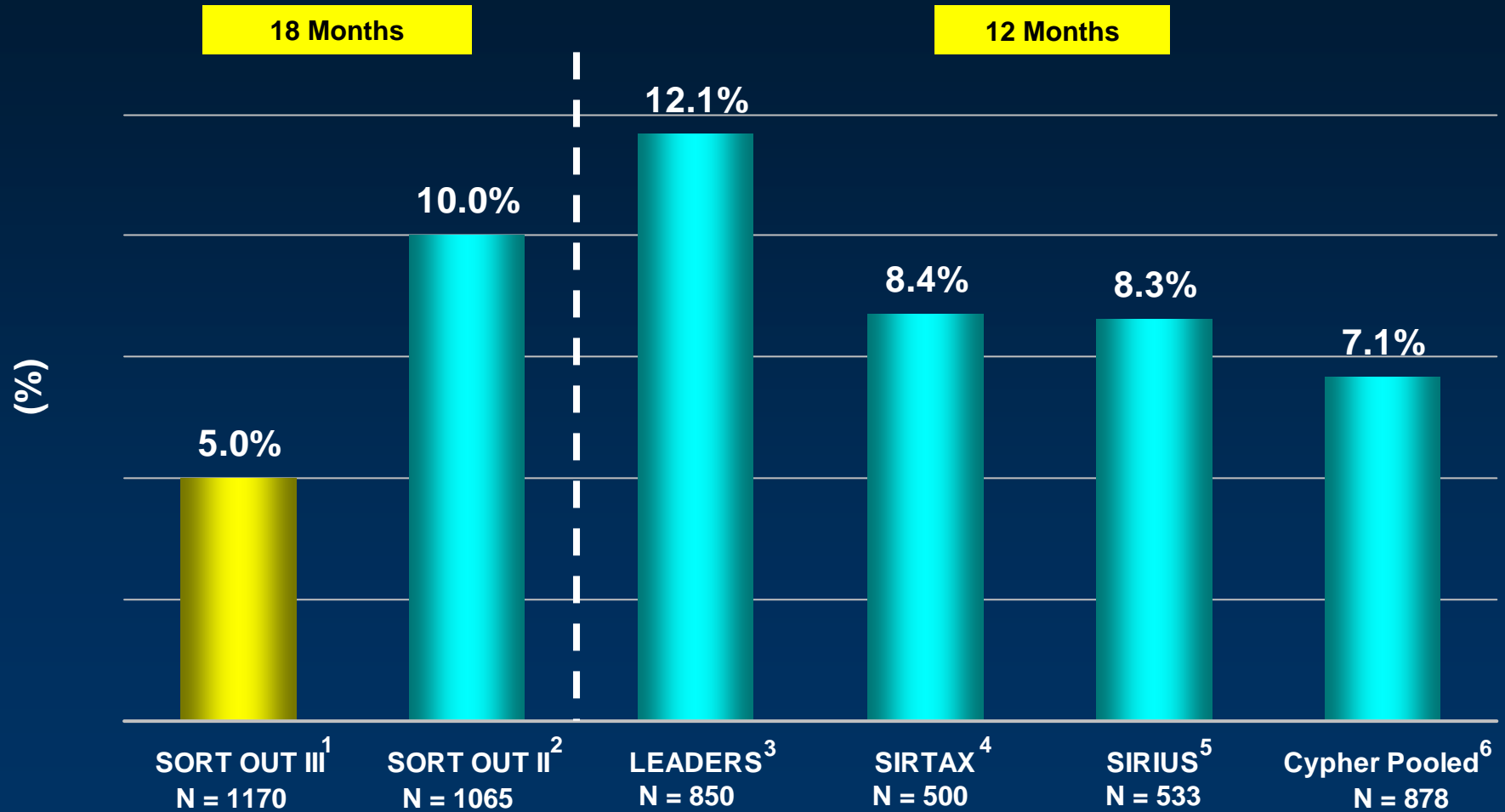
⁴ Räber L et al., TCT2009

⁵ Weisz G et al., JACC, 53 pp. 1488-1497, 2009.

⁶ Caixeta A et al., JACC, 54 pp. 894-902, 2009.

Cypher: SORT OUT III MACE

Inconsistent Clinical Evidence



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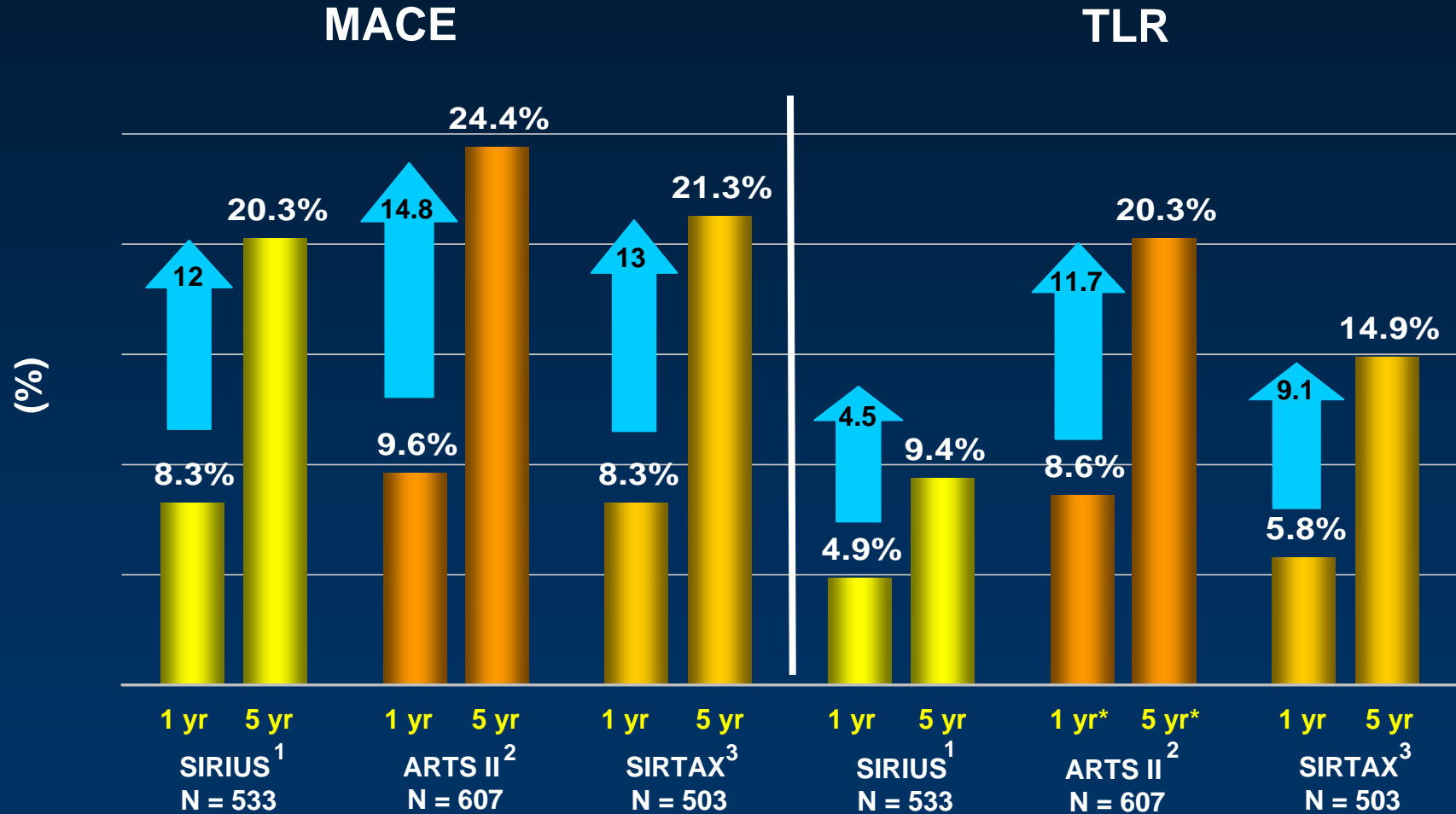
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Cypher: Long-Term Endpoint Increases

MACE and TLR Increase from 1 – 5 Yr



¹ Weisz G et al., JACC, 53 pp. 1488-1497, 2009.

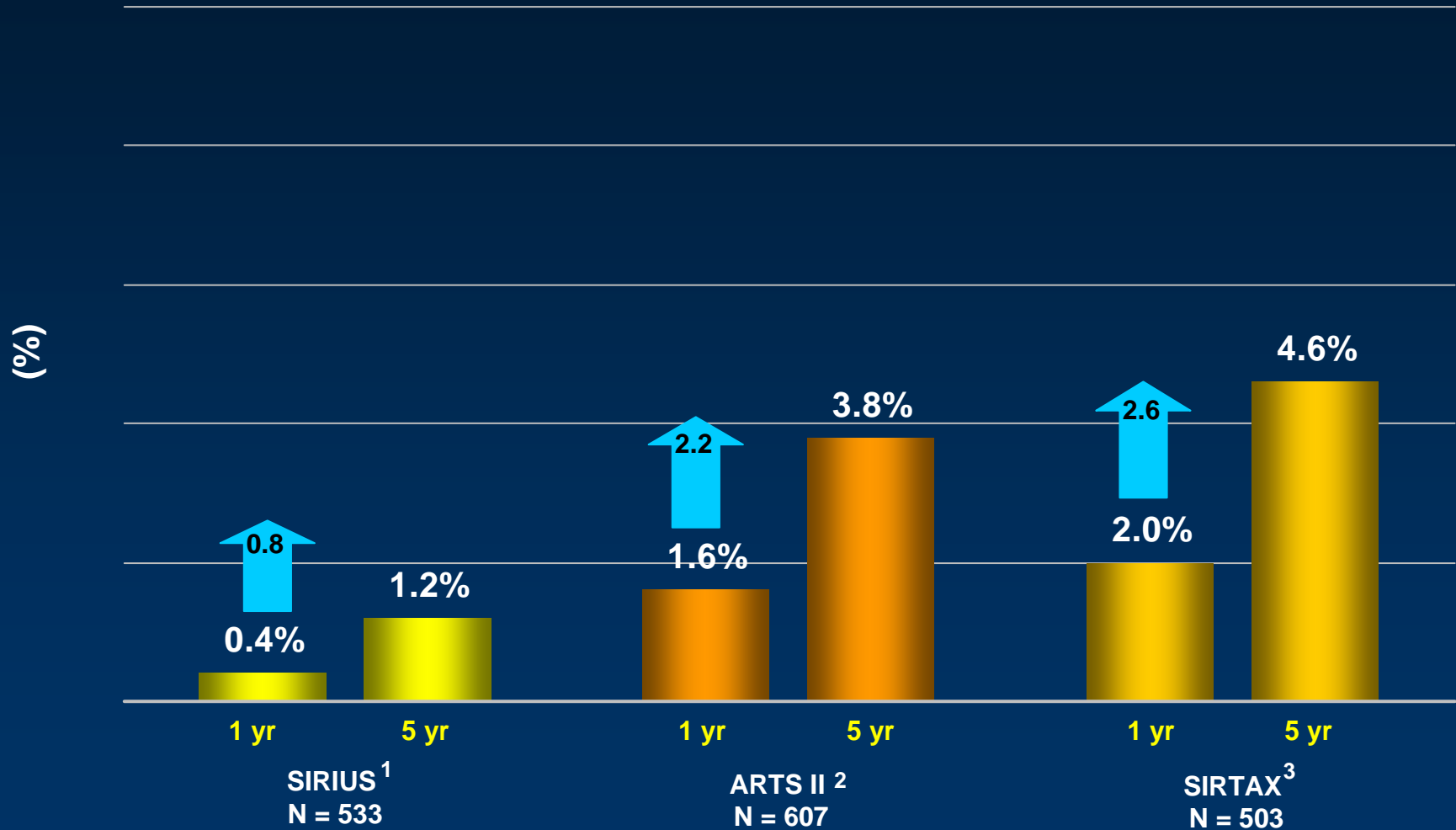
² Serruys P et al., EuroInterv, 1 pp. 147-156, 2005. Serruys P et al., JACC, 55 pp. 1093-1101, 2010.

³ Räber L et al., TCT2009

* Total revascularization

Cypher: Long-Term Endpoint Increases

ARC Definite ST Increases from 1 – 5 Yr



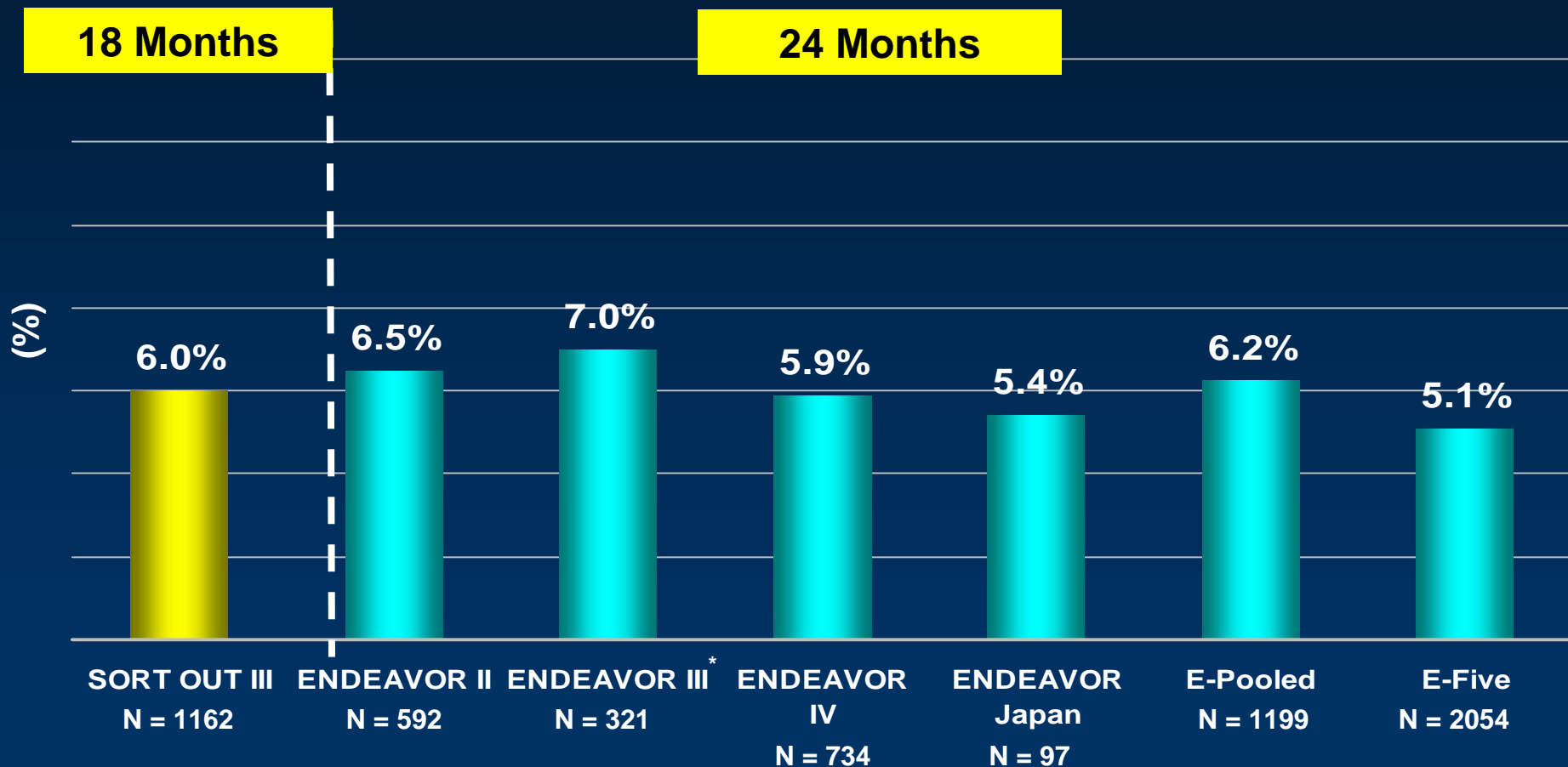
¹ Weisz G et al., JACC, 53 pp. 1488-1497, 2009.

² Serruys P et al., JACC, 55 pp. 1093-1101, 2010.

³ Räber L et al., TCT2009

Endeavor: SORT OUT III TLR

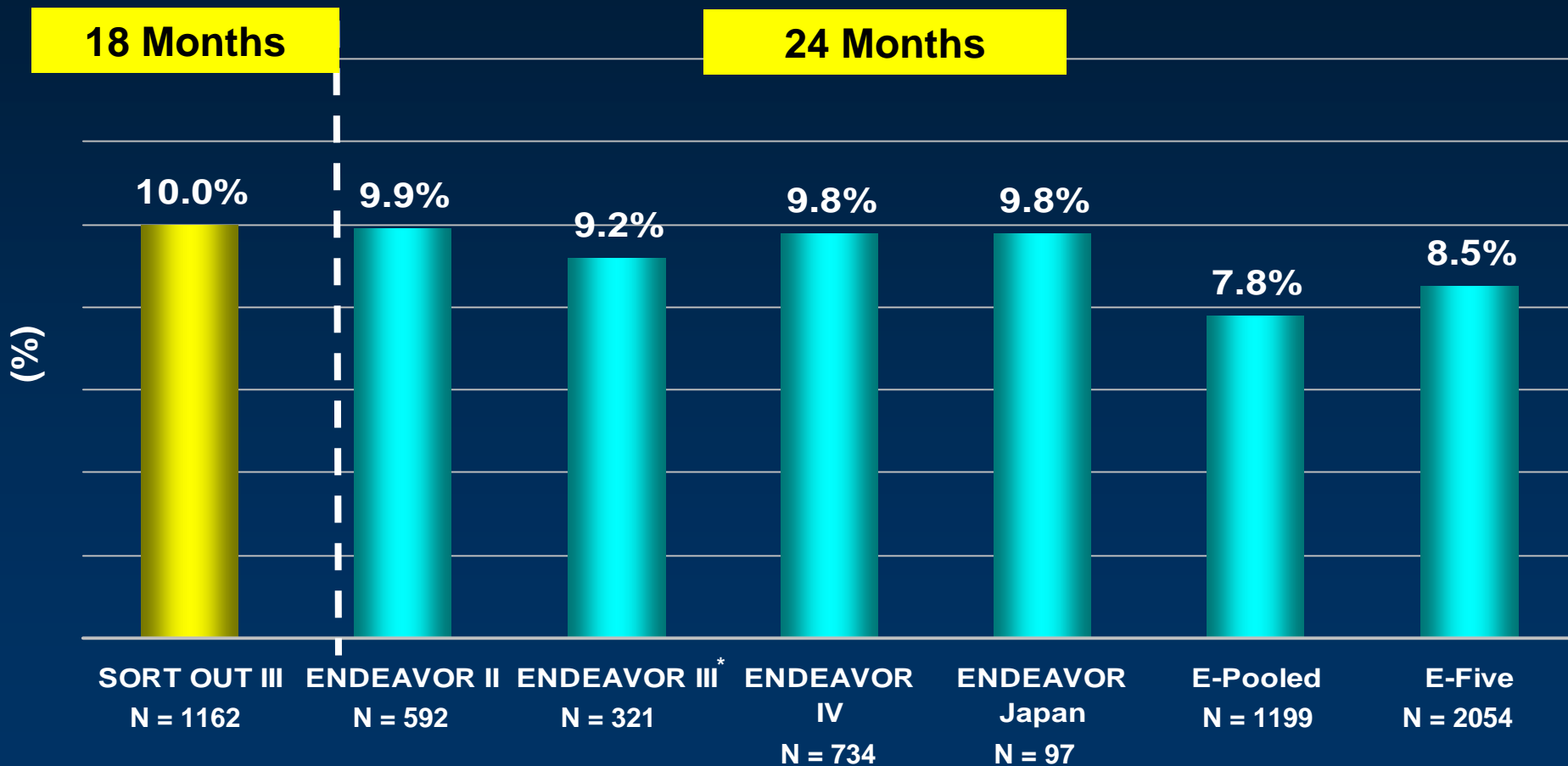
Consistent Clinical Evidence



* ENDEAVOR III included angiographic follow-up in all patients.
ENDEAVOR Pooled Analysis: E I (5 yr), E II (5 yr), E II CA (5 yr), E III (5 yr), E IV (3 yr) and E pK (3 yr).

Endeavor: SORT OUT III MACE

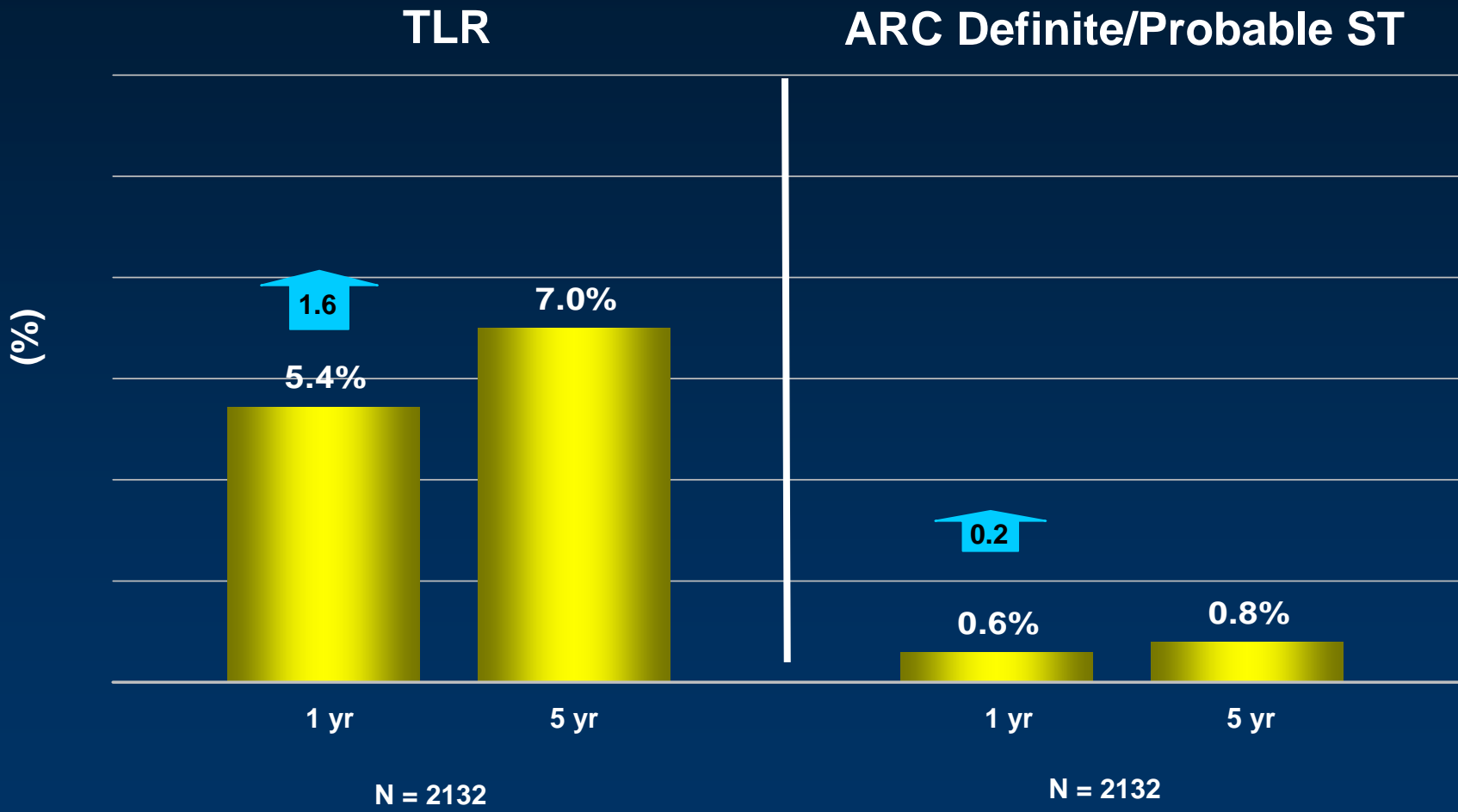
Consistent Clinical Evidence



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ENDEAVOR Pooled Analysis

TLR and ARC Def/Prob ST From 1 – 5 Yr

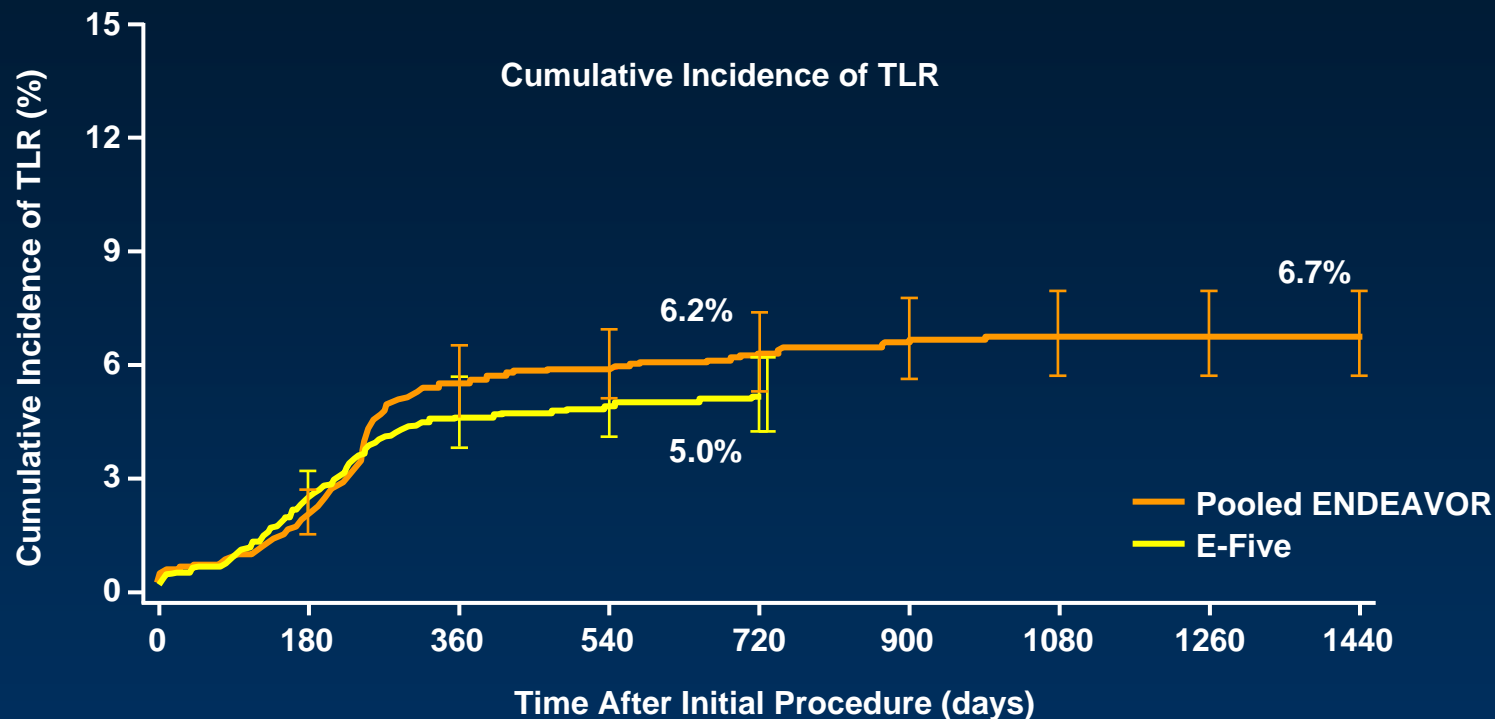


SORT OUT III Perspectives

- **Concerns with SORT OUT III Methodology:** The SORT OUT III study uses an unconventional methodology that raises questions regarding the reproducibility and viability of the results
- **Inconsistency of Data for Cypher:** SORT OUT III shows unexpectedly low rates and inconsistent data for Cypher compared with nearly every other trial utilizing the Cypher stent
- **SORT OUT III Results Are Short-Term Only:** The long-term deficiencies of Cypher demonstrated in multiple studies are not addressed by the short-term focus of SORT OUT III
- **Consistency of Data for Endeavor:** While the SORT OUT III data are inconsistent for Cypher, the Endeavor outcomes in SORT OUT III reinforce the low and durable event rates for the Endeavor stent

Endeavor: Durable TLR Rates

Real-World Experience Consistent with Pooled Analysis

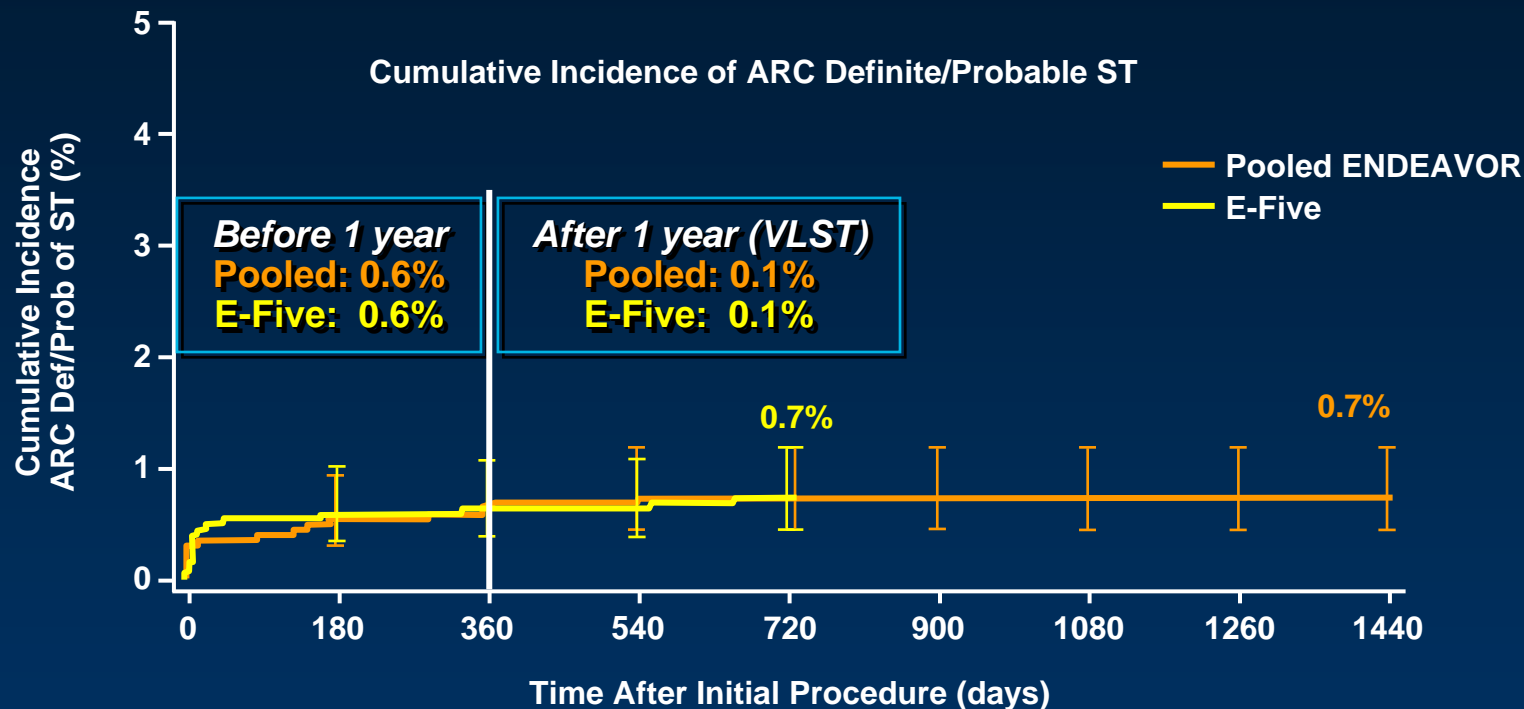


Days	0	180	360	540	720	730	900	1080	1260	1440
No. at Risk	2133	2130	2061	1939	1895	1557	1169	1150	1015	858
% CI	0.1	1.8	5.4	5.8	6.2	6.2	6.5	6.7	6.7	6.7
No. at Risk	2116	2113	2046	1974	1924	1816				
% CI	0.0	2.3	4.5	4.8	5.0	5.0				

ENDEAVOR Pooled Analysis: E I (5 yr), E II (4 yr), E II CA (4 yr), E III (3 yr), E IV (2 yr) and E pK (2 yr).
The 2-year follow-up rate for Pooled Analysis was measured at 720 days and for E-Five at 730 days.

Endeavor: Low Rates of ARC Def/Prob ST

Real-World Experience Consistent with Pooled Analysis



Days	0	180	360	540	720	730	900	1080	1260	1440
No. at Risk	2133	2131	2089	2036	1995	1650	1241	1225	1087	909
% CI	0.0	0.5	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.7
No. at Risk	2116	2113	2086	2060	2014	1906				
% CI	0.0	0.6	0.6	0.6	0.7	0.7				

ENDEAVOR Pooled Analysis: E I (5 yr), E II (4 yr), E II CA (4 yr), E III (3 yr), E IV (2 yr) and E pK (2 yr).
 The 2-year follow-up rate for Pooled Analysis was measured at 720 days and for E-Five at 730 days.

Indications

The Endeavor Sprint Zotarolimus-Eluting Coronary Stent 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

Use of 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 who can not 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 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 ENDEAVOR stent 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, myocardial infarction or all-cause mortality. Additional data from longer-term follow-up in the randomized clinical trials on the Endeavor stent and analyses of DES-related stent thrombosis are expected and should be considered in making treatment decisions as data become available.
- When drug-eluting stents 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 drug-eluting stents 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, myocardial infarction or death.

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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 27mm 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; late or very late thrombosis; infection or fever; 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; and 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, circumoral paresthesia, diarrhea, dry skin, headache, hematuria, infection, injection site reaction, pain (abdominal, arthralgia, injection site), and 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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