SORT OUT III

Perspectives on 3-Year Results

SORT OUT III 3-Year Results—Perspectives

Cypher® DES:

Notable increase in event rates out to 3 years

- **124% increase in MACE between 18–36 months (4.5–10.1%)**
- **129% increase in TLR between 18–36 months (1.7–3.9%)**
  - **Significantly higher VLST vs. Endeavor® DES at 3 years (1.1% *vs.* 0%, *p = 0.0005*) driven by 12 VLST cases reported for Cypher DES (ARC definite)**

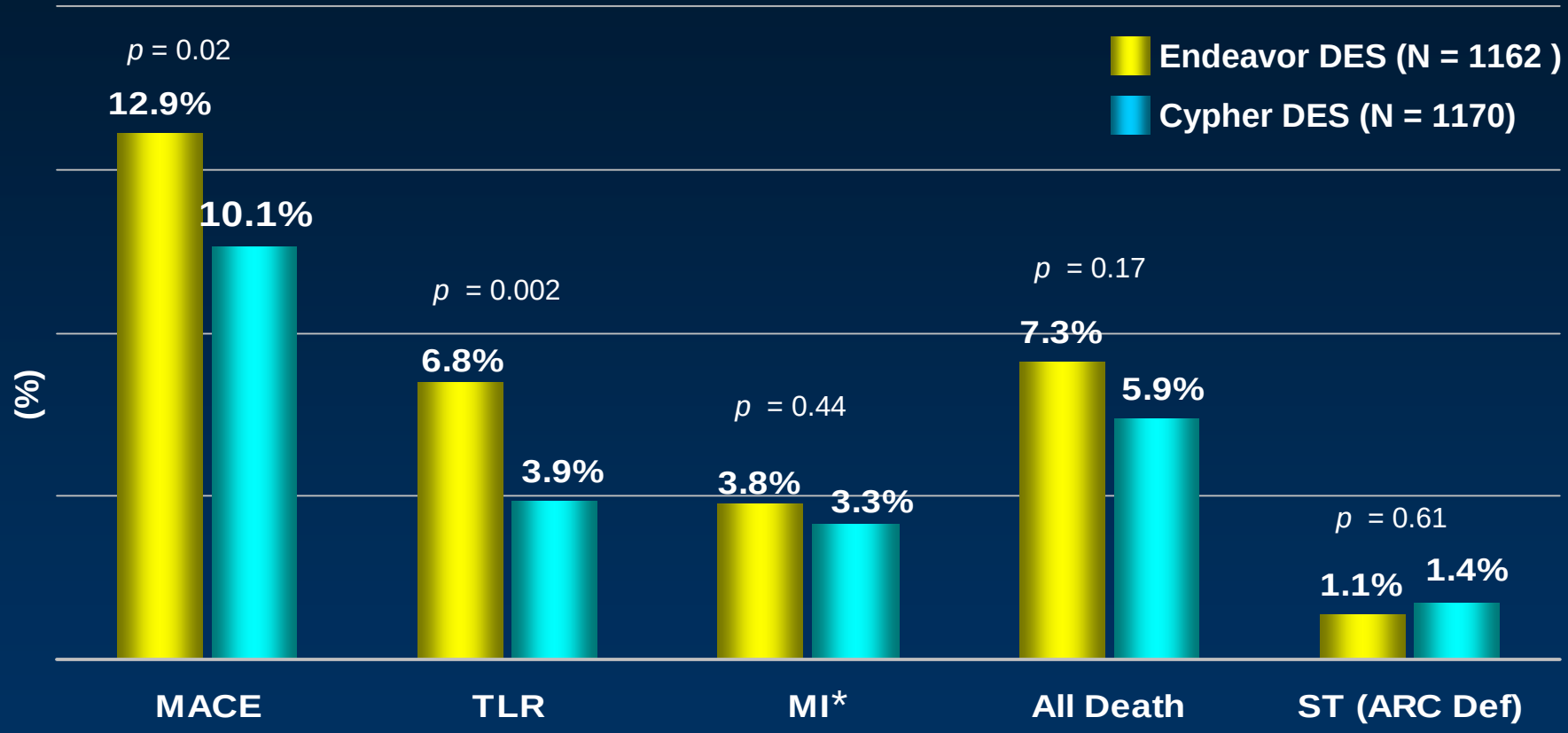
Endeavor DES:

Long-term efficacy and safety performance confirmed

- **Endeavor DES shows lower rates of increase across all endpoints from 18–36 months vs. Cypher DES**
- **No VLST (ARC definite) out to 3 years**
- **Reassuring long-term performance consistent with ENDEAVOR trials**

SORT OUT III

Event rates at 3 years



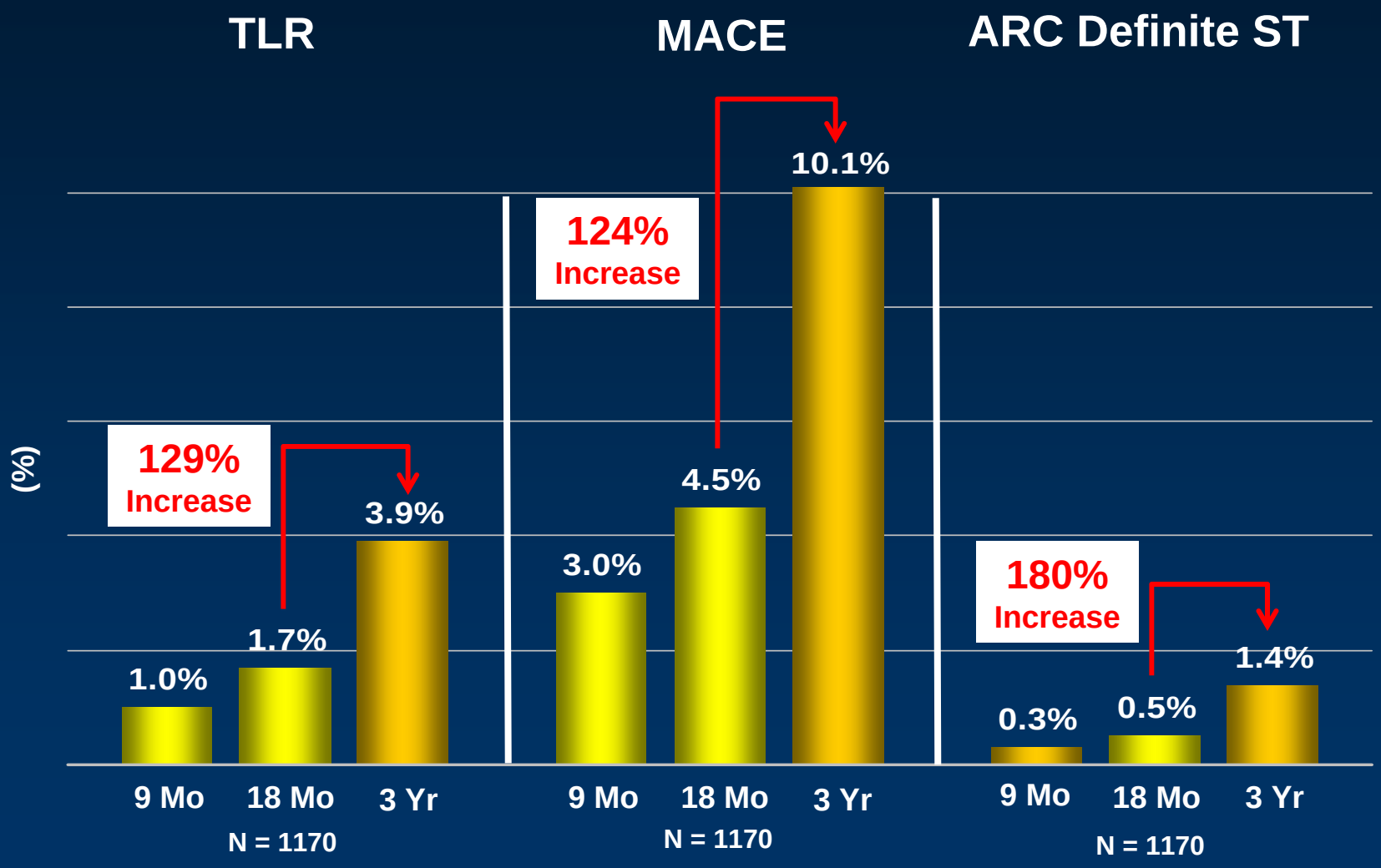
Statistical difference in MI and All Death observed at 18 months disappears at 3 years.

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

Maeng M et al. ACC 2011.

Cypher DES: Notable Increase in Event Rates

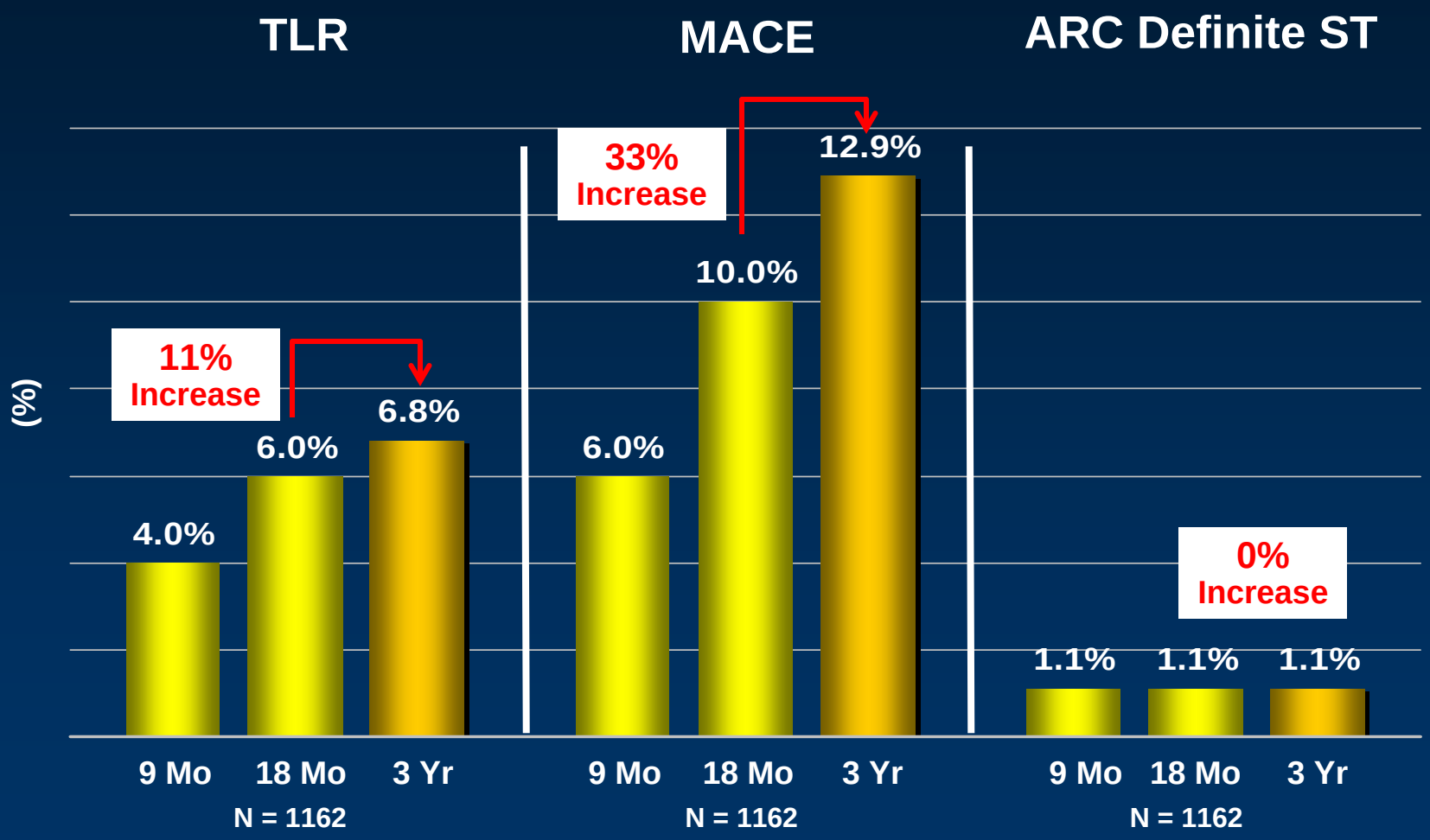
TLR, MACE and stent thrombosis from SOIII out to 3 years



Maeng M et al. ACC 2011.

Endeavor DES: Reassured Long-Term Performance

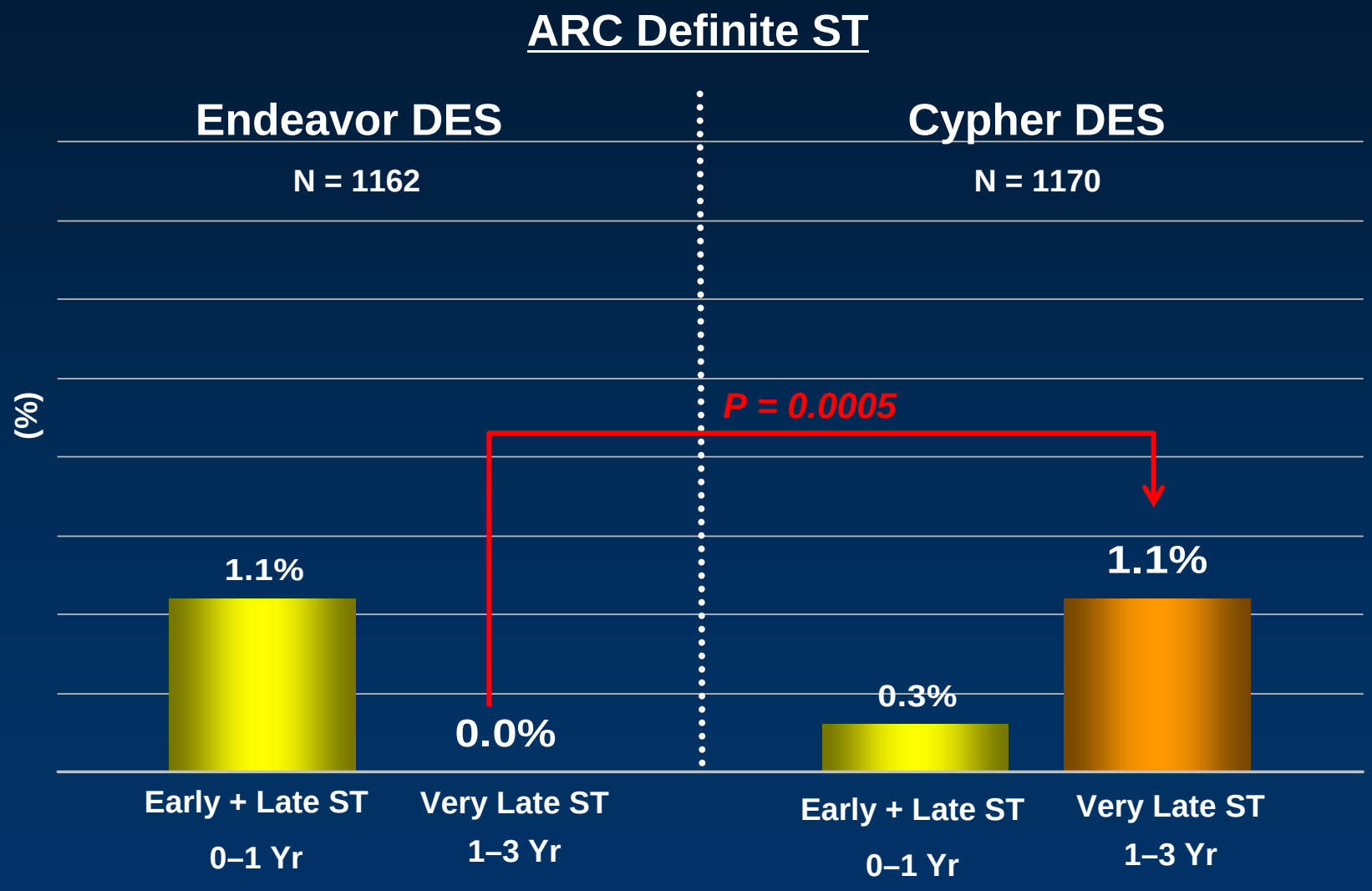
TLR, MACE and stent thrombosis from SOIII out to 3 years



Maeng M et al. ACC 2011.

Endeavor DES: Reassured Long-Term Performance

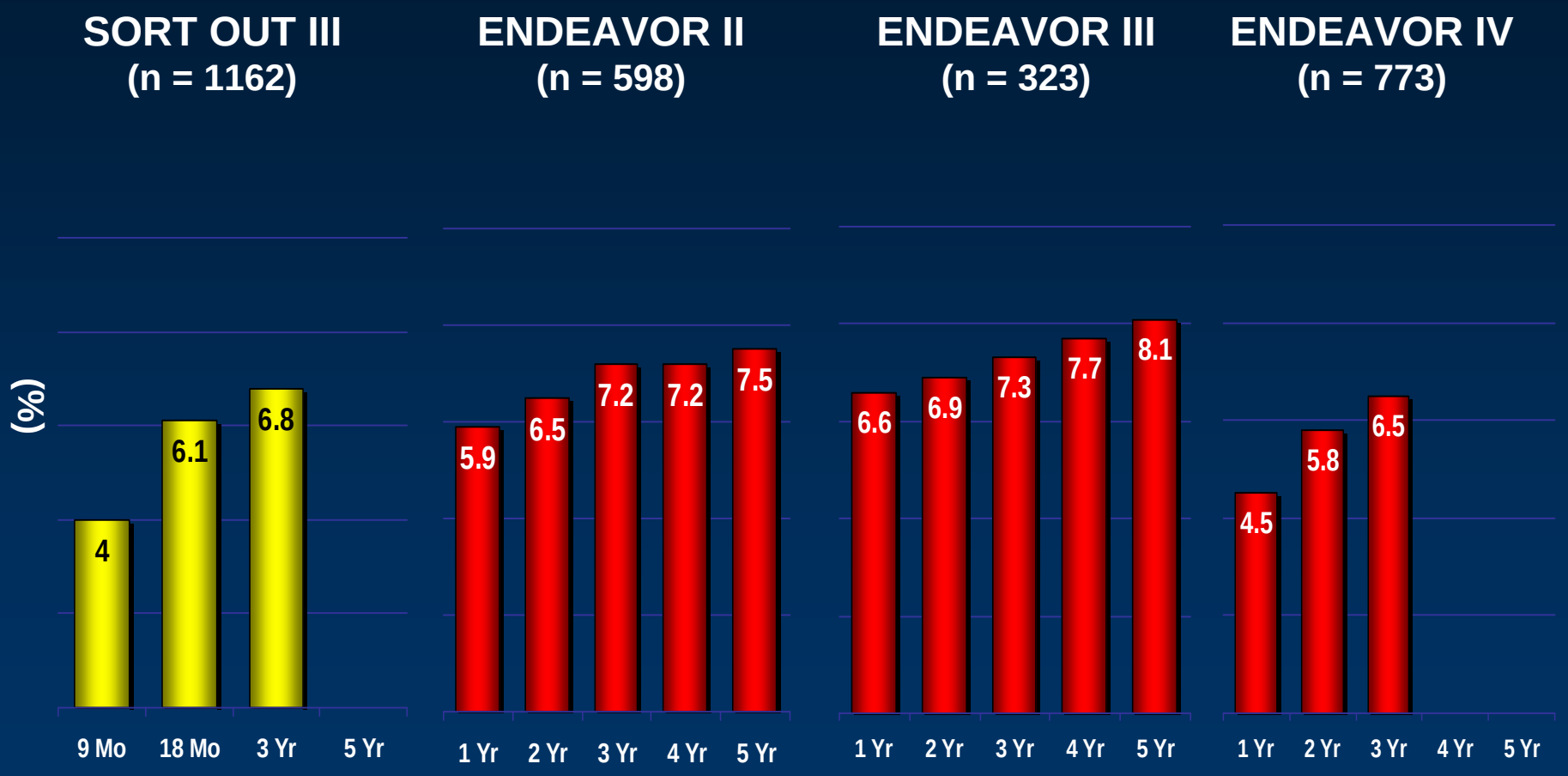
0% very late stent thrombosis rate out to 3 years



Maeng M et al. ACC 2011.

Endeavor DES: Reassured Long-Term Performance

Consistent and durable TLR rates



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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 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.

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Appendix

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 DES and a low rate with Endeavor DES*

5. Differences in patient adherence to DAPT regimens were not reported despite the potential effect on safety outcomes

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