A Prospective, Randomized, "All-Comers" Trial of Biodegradable Polymer-Coated Biolimus-Eluting Stents vs. Biocompatible Polymer-Coated Zotarolimus-Eluting Stents

The SORT OUT VI Trial

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Disclosure Statement of Financial Interest

I, Bent Raungaard DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Background

- Compared with bare metal stents, first-generation drug-eluting stents showed reduced risk of restenosis, but the risk of stent thrombosis was a concern.
- Newer-generation drug-eluting stents have been designed to improve efficacy, safety, and device performance.
- Biocompatibility has been improved by use of durable polymers with enhanced biocompatibility or biodegradable polymers.
- There are no large scale randomized comparison studies of biodegradable polymer-coated BioMatrix Flex stents and biocompatible polymer-coated Resolute Integrity stents in all-comer populations.

Objective

To compare the safety and efficacy of the zotarolimus-eluting Resolute Integrity stent with the biolimus-eluting BioMatrix Flex stent in a population-based setting.

ClinicalTrials.gov Identifier: NCT 01956448

Method

- The trial was performed within the framework of the Scandinavian Organization for Randomized Trials with Clinical Outcome (SORT OUT).
- The trial was designed to reflect daily clinical practice. Therefore, no control angiography or study related patient contact were scheduled.
- We used patient driven clinical event detection, through data from Danish health care registries.

Patient Population

Study period: March 2011 to August 2012

Criteria of inclusion

- 18 years of age or older.
- Chronic stable coronary artery disease or acute coronary syndromes.
- At least one coronary lesion with more than 50% diameter stenosis in a vessel with a reference diameter of 2.25 to 4.0 mm.

No restrictions were placed on number of treated lesions or treated vessels or lesion length.

Patient Population

Study period: March 2011 to August 2012

Criteria of exclusion

- Life expectancy less than one year.
- Allergy to aspirin, clopidogrel, prasugrel, ticagrelor, zotarolimus, or biolimus.
- Unacceptable risk by 12-month dual antiplatelet treatment.
- Inability to provide written informed consent.

Primary Endpoint

Major Adverse Cardiac Events at 12 months

Composite of

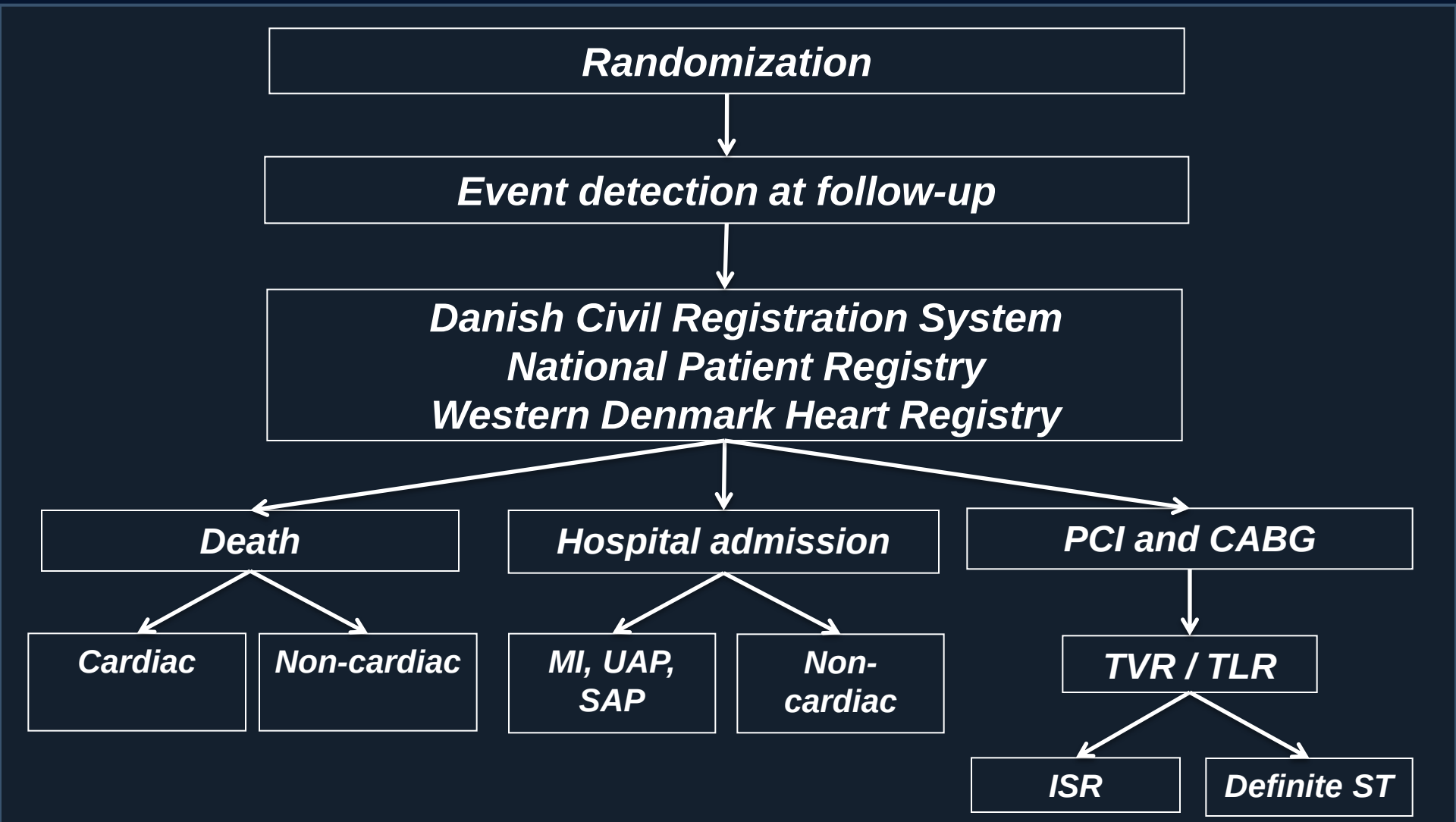
- cardiac death
- myocardial infarction (not clearly attributable to a non-target lesion)
- target lesion revascularization

Statistical Assumptions

Power calculation

- Non-inferiority design
- Estimated 12-month event rate:
  - zotarolimus-eluting stent group 0.08
  - biolimus-eluting stent group 0.05
- Non-inferiority margin: 0.025
- One-sided type I error: 0.05
- Power 90%
- Number of patients 3000

Clinical Event Detection



Patient Characteristics

	ZOTAROLIMUS-ELUTING STENT	BIOLIMUS-ELUTING STENT	p
No. of patients	1502	1497	
Age (years)	65.7 ±10.7	65.8 ±10.9	0.66
Men (%)	76.2	75.8	0.82
Diabetes (%)	17.6	18.0	0.78
Hypertension (%)	59.7	58.1	0.38
Lipid-lowering therapy (%)	59.3	59.1	0.95
Current smoker (%)	30.7	30.7	0.97
Prior CABG (%)	8.4	6.8	0.09
Prior PCI (%)	18.7	22.0	0.03
Prior myocardial infarction (%)	18.7	19.7	0.52
Body mass Index (kg/m^2)	26.9	26.9	0.97

Patient Characteristics

	ZOTAROLIMUS-ELUTING STENT	BIOLIMUS-ELUTING STENT	p
No. of patients	1502	1497	
Indication for PCI (%)			0.11
Stable angina	45.6	44.8	
NSTEMI / unstable angina	31.0	33.9	
STEMI	19.6	16.9	
Other	3.8	4.4	

Lesion Characteristics

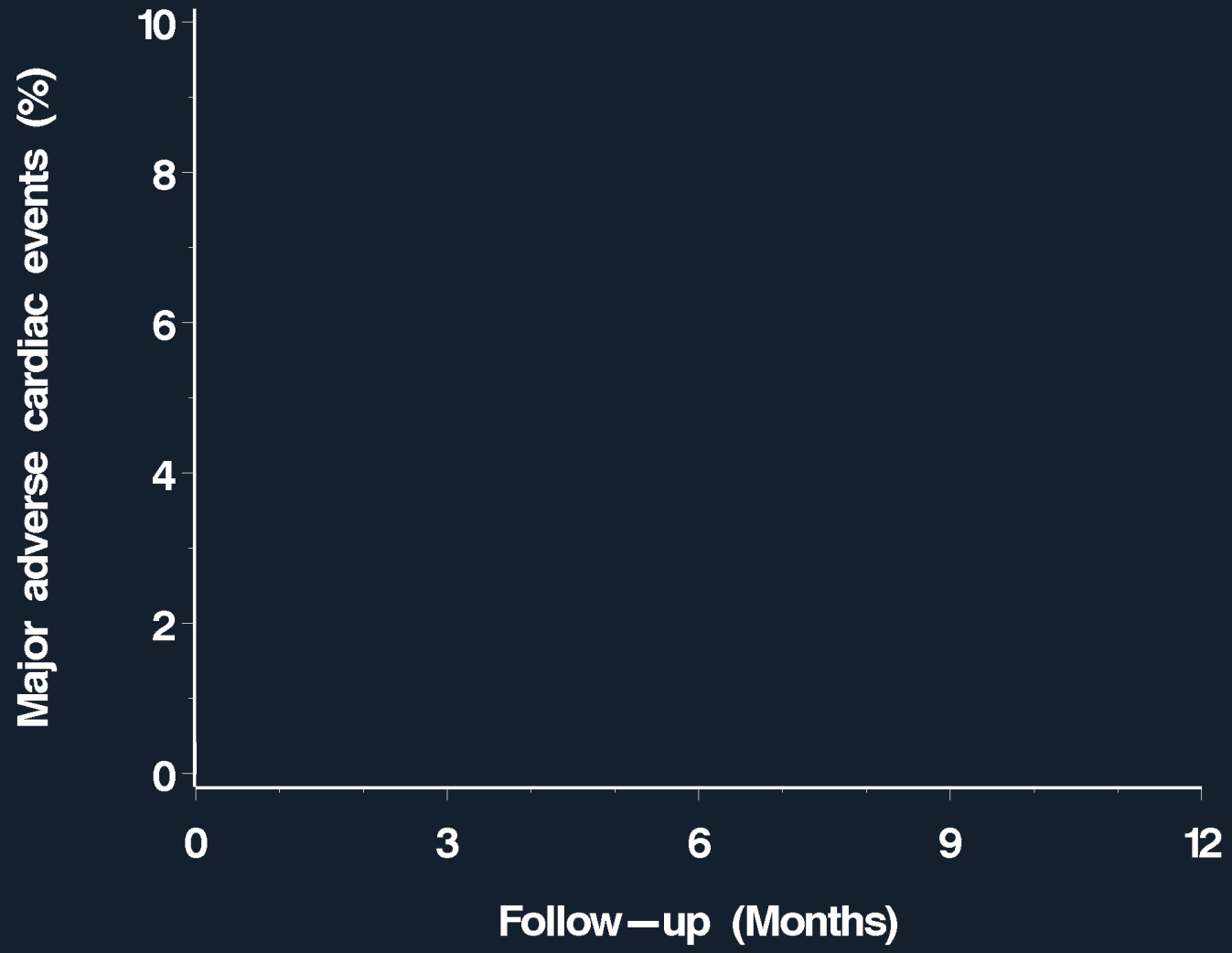
	ZOTAROLIMUS-ELUTING STENT	BIOLIMUS-ELUTING STENT	p
No. of lesions	1880	1791	
Target vessel location (%)			0.72
Left main	0.9	1.2	
Left anterior descending	40.2	41.5	
Left circumflexus	23.8	24.0	
Right coronary	33.9	32.3	
Saphenous vein graft	1.2	1.0	
Lesion type B2/C (%)	61.5	58.2	0.06
Reference vessel size (mm)	3.2 (2.9 - 3.5)	3.0 (2.8 - 3.5)	0.10

Lesion Characteristics

	ZOTAROLIMUS-ELUTING STENT	BIOLIMUS-ELUTING STENT	p
No. of lesions	1880	1791	
Patients with > 1 lesion (%)	25.3	22.1	0.04
Patients with > 1 stent (%)	35.9	32.6	0.06
Total stent length per patient (mm)	21.0 (15.0 - 3.0)	18.0 (14.0 - 29.0)	<0.01
Maximum pressure (atm)	16.0 (12.0 - 18.0)	16.0 (12.0 - 18.0)	0.19
Stent delivery failure (%)	1.7	2.1	0.34
Use of GP IIb/IIIa inhib. (%)	4.8	5.2	0.60

1º Endpoint: Major Adverse Cardiac Events

(cardiac death, myocardial infarction, target lesion revascularization)



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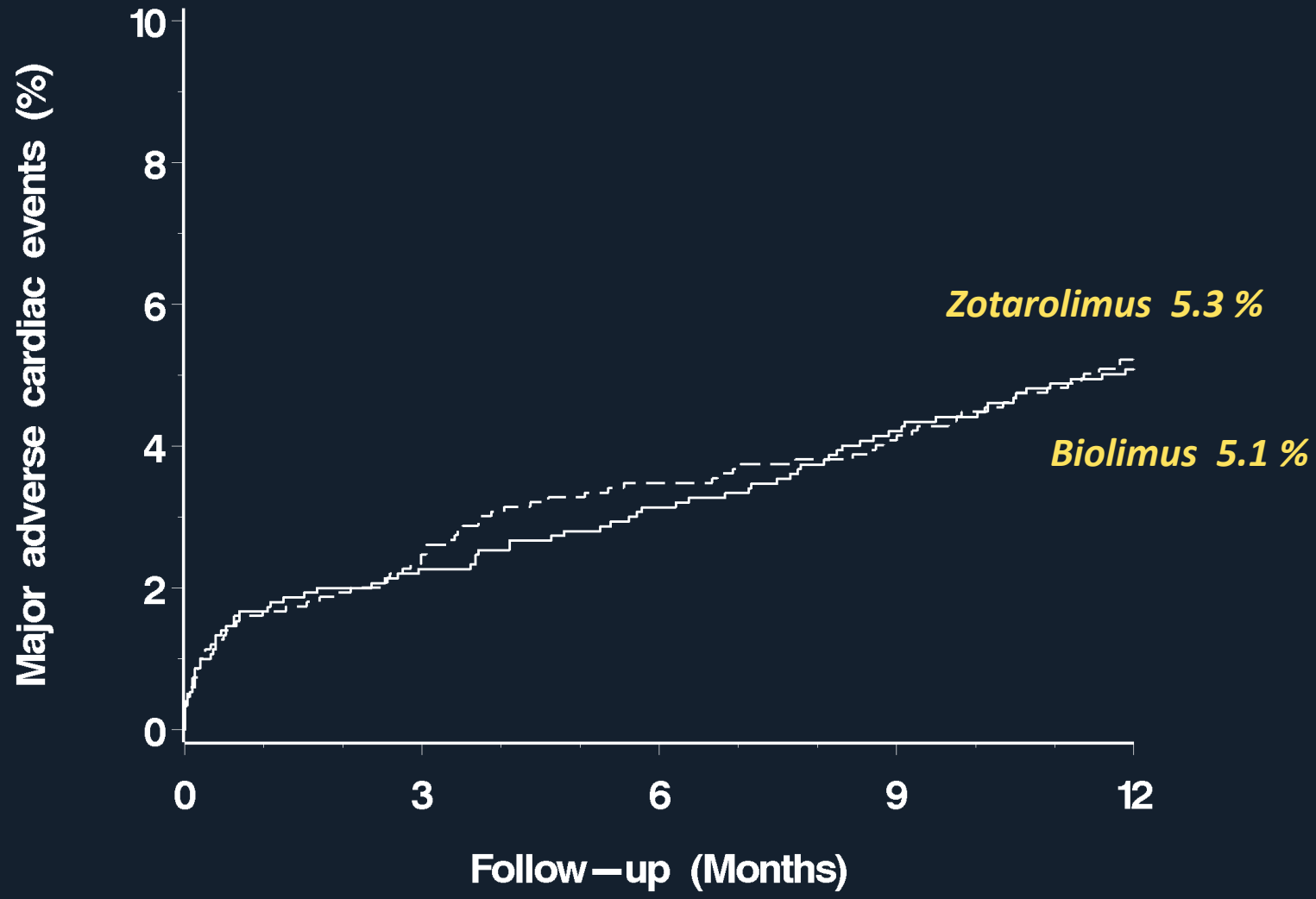


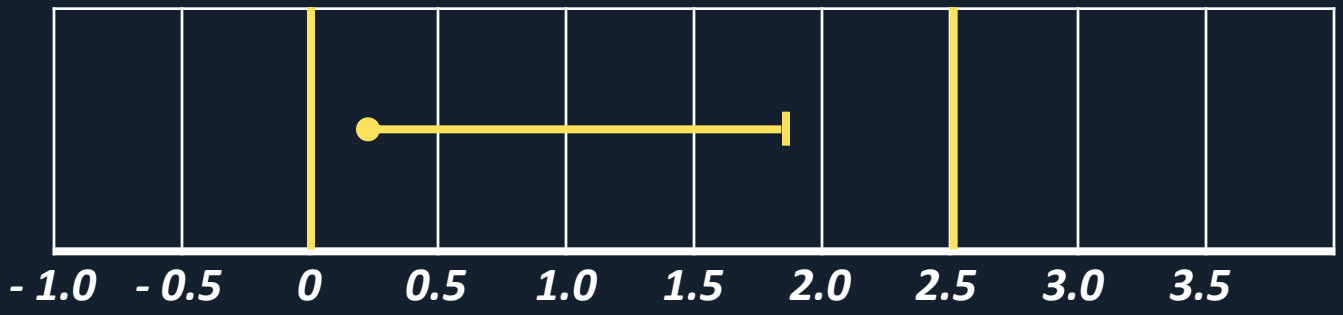
1º Endpoint: Major Adverse Cardiac Events

(cardiac death, myocardial infarction, target lesion revascularization)

ZES 5.3% vs. BES 5.1%

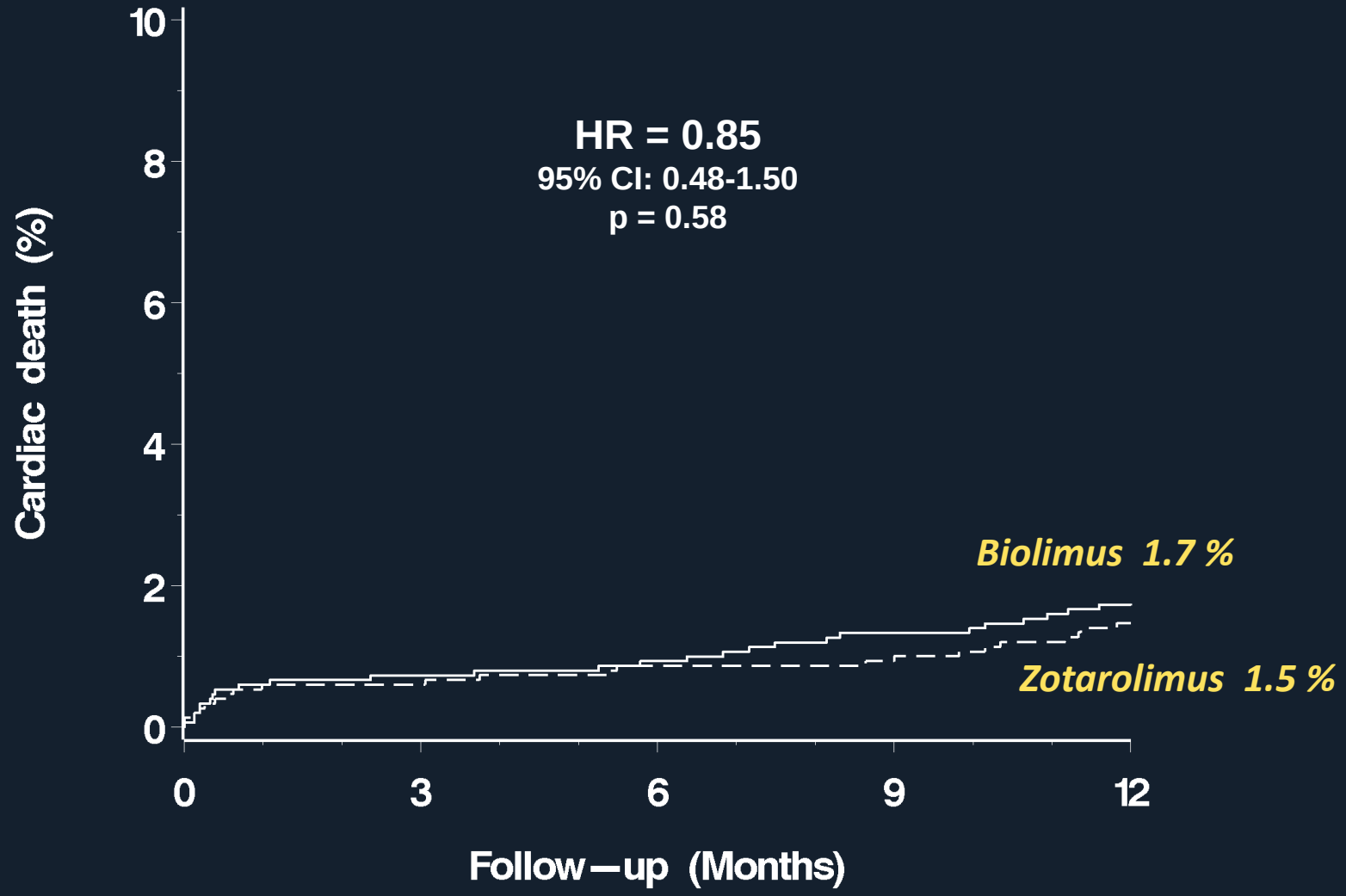
$P_{non\text{-}inferiority}$ = 0.006

Difference:	***0.2%***
Upper one-sided 95% CI:	***1.8%***



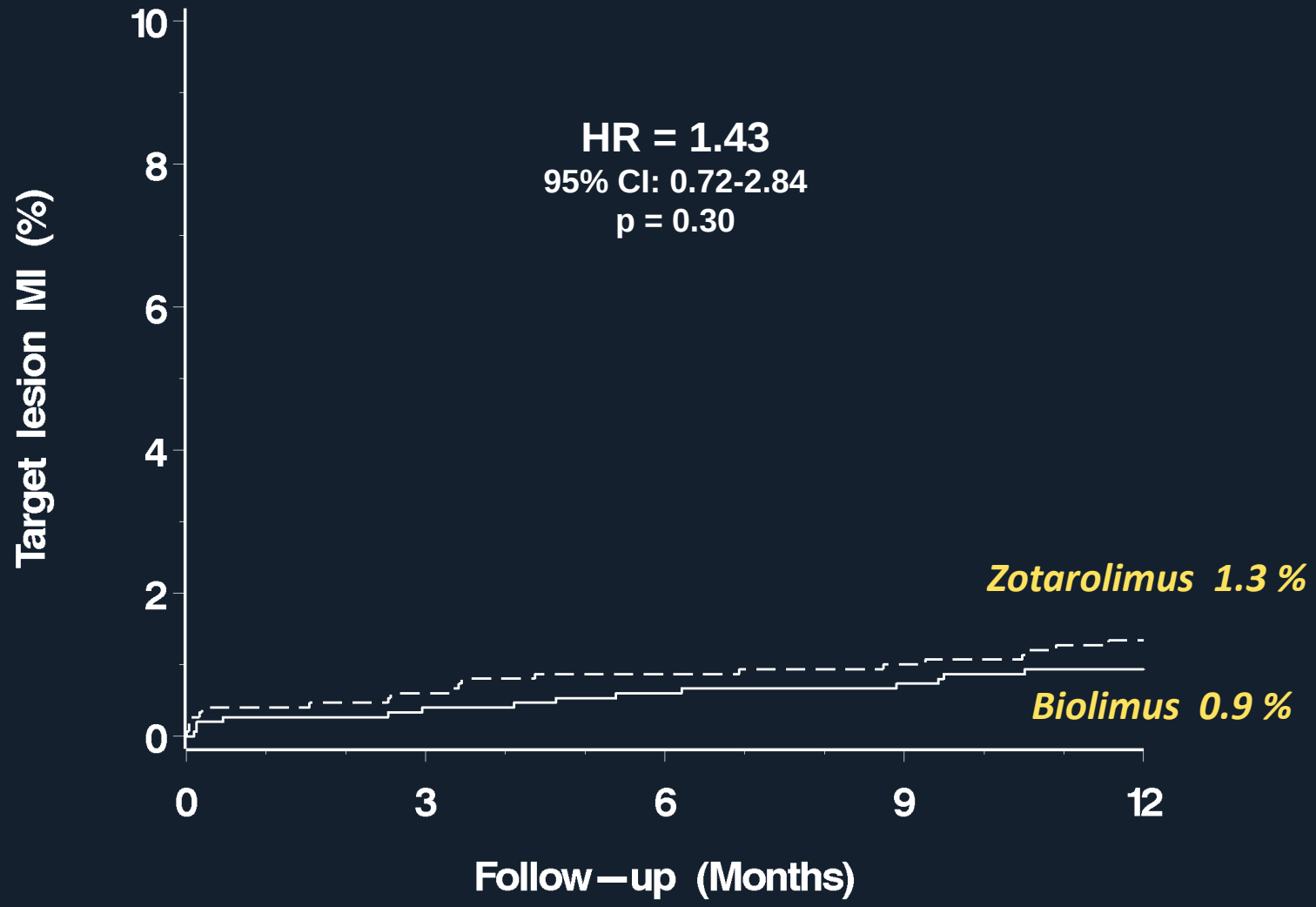
ZES was non-inferior to BES

Cardiac Death

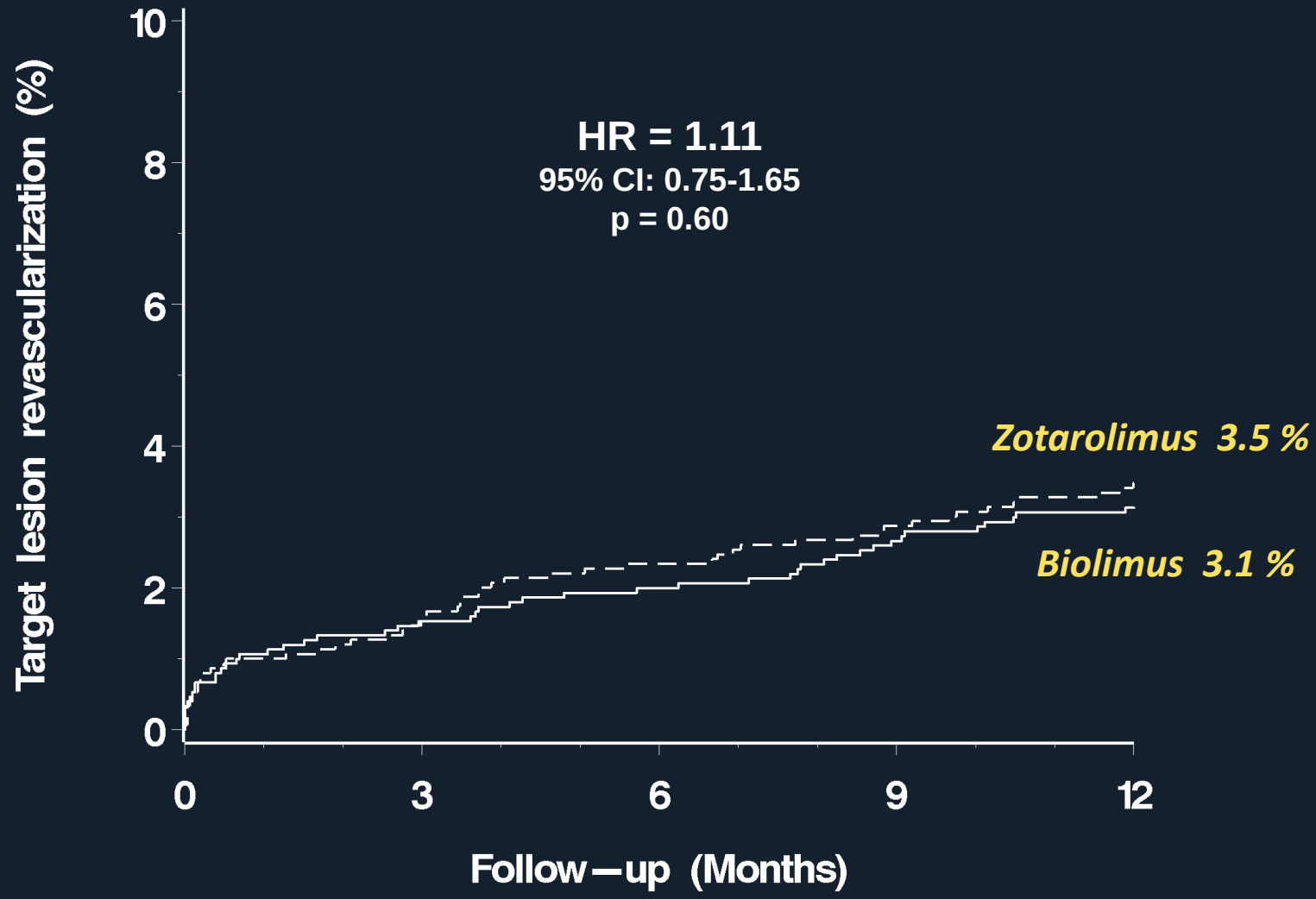


Myocardial Infarction

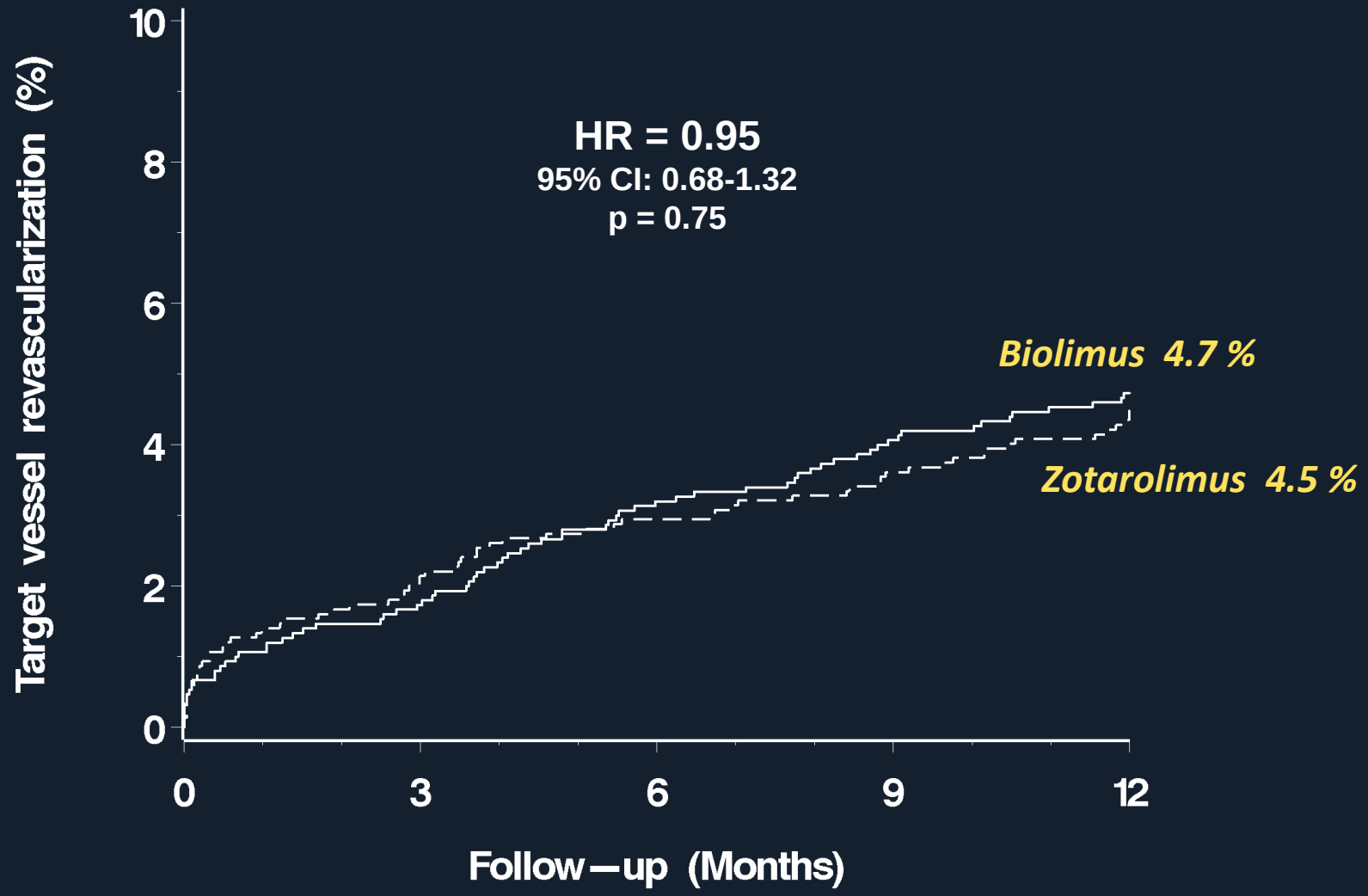
(not clearly attributable to a non-target lesion)



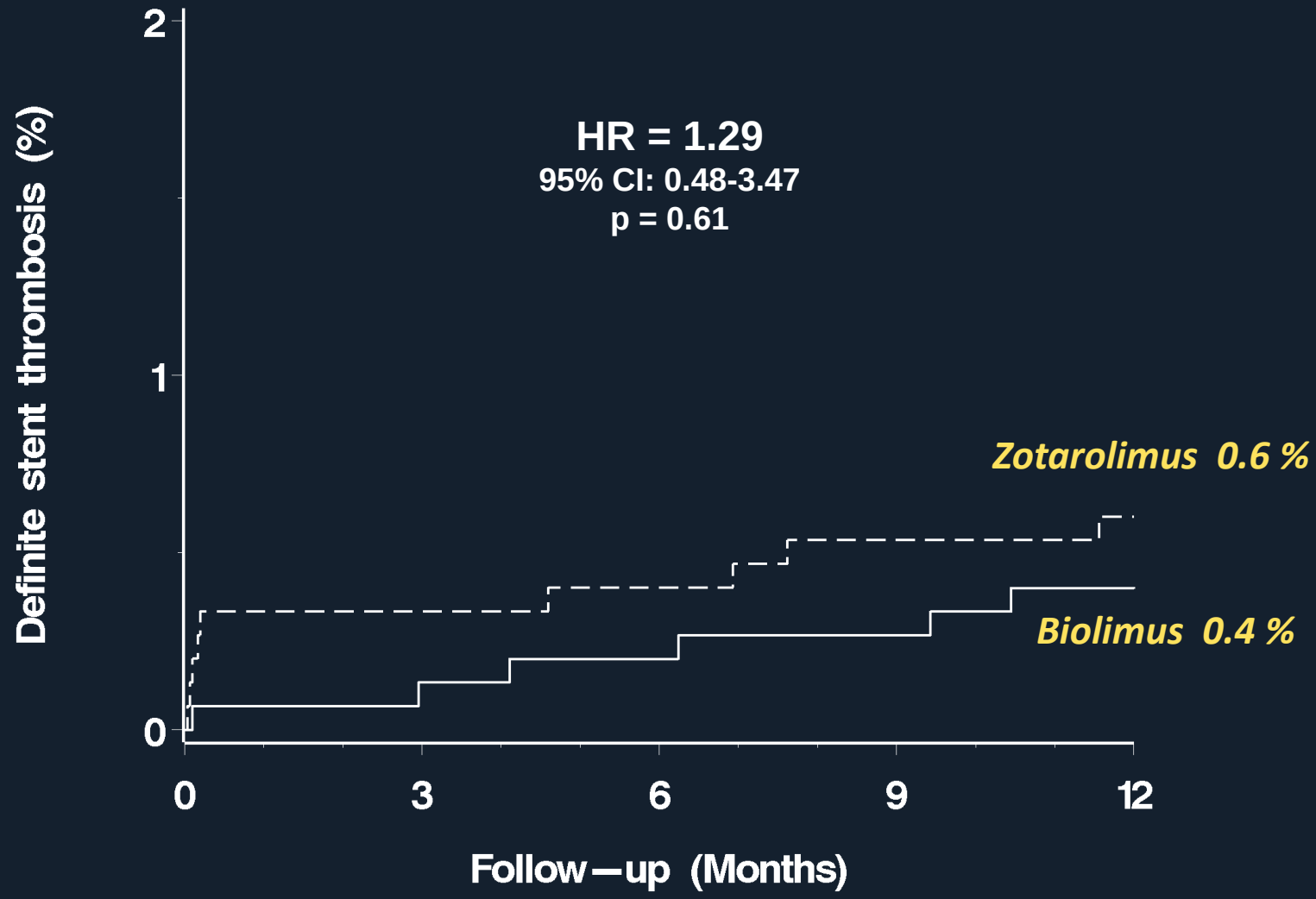
Target Lesion Revascularization



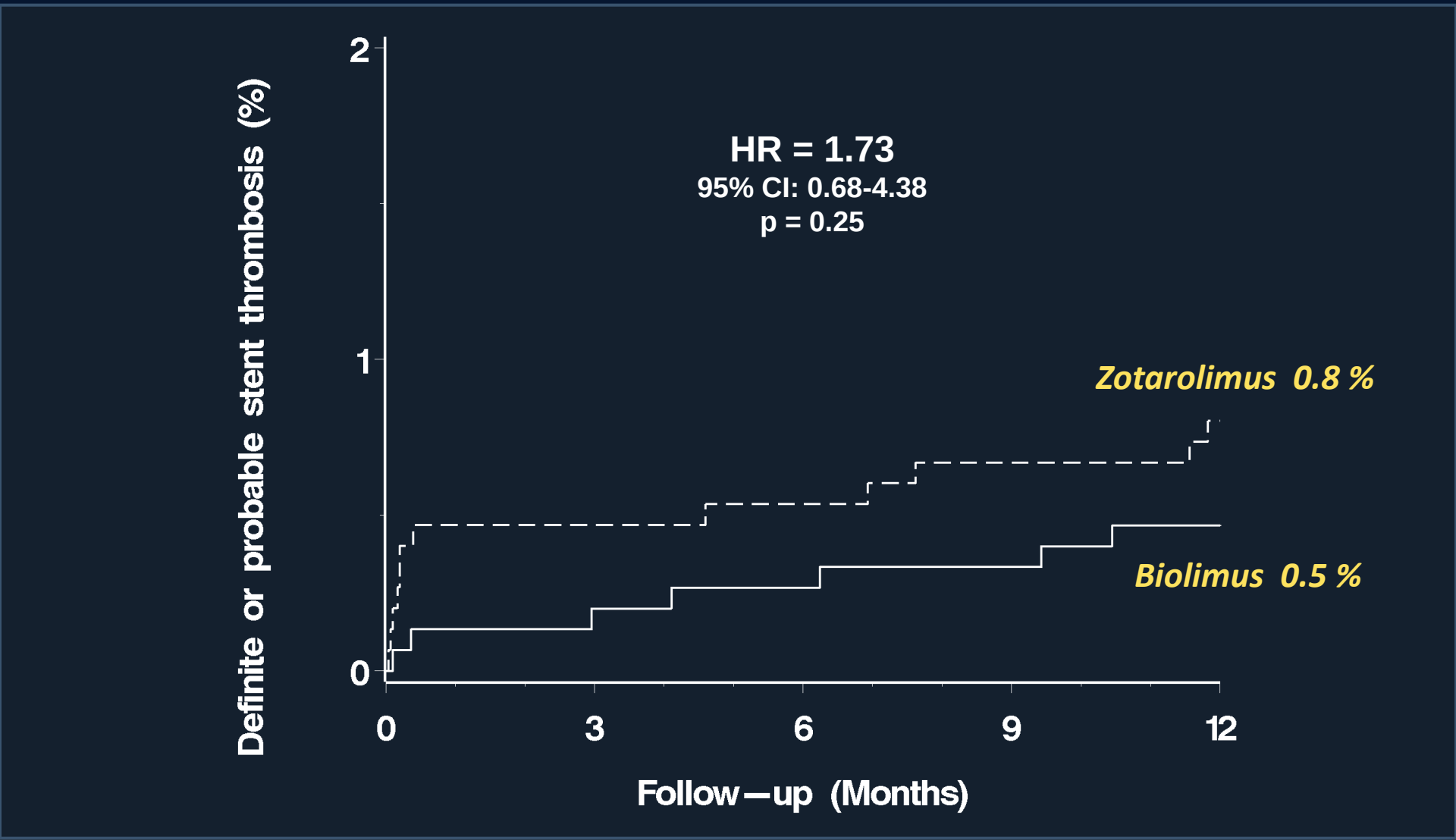
Target Vessel Revascularization



Definite Stent Thrombosis



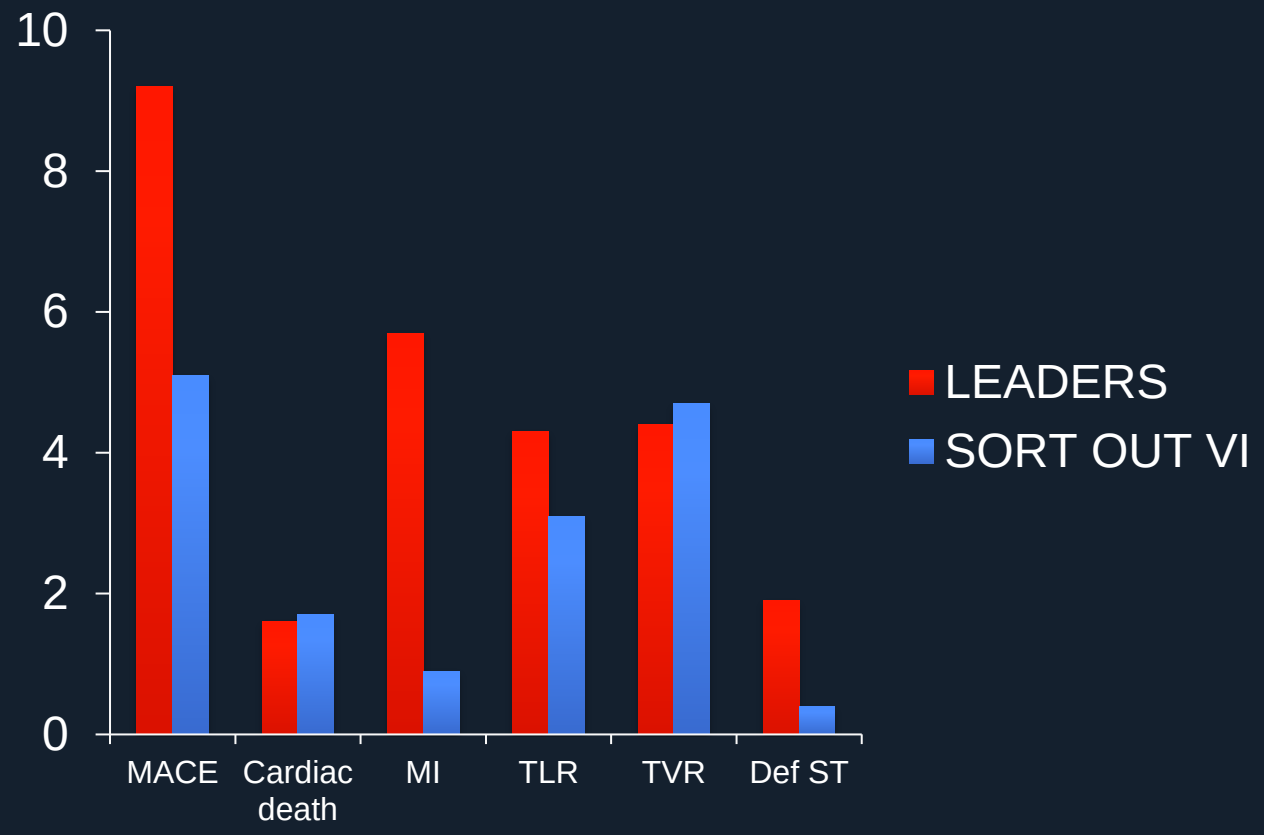
Definite or Probable Stent Thrombosis



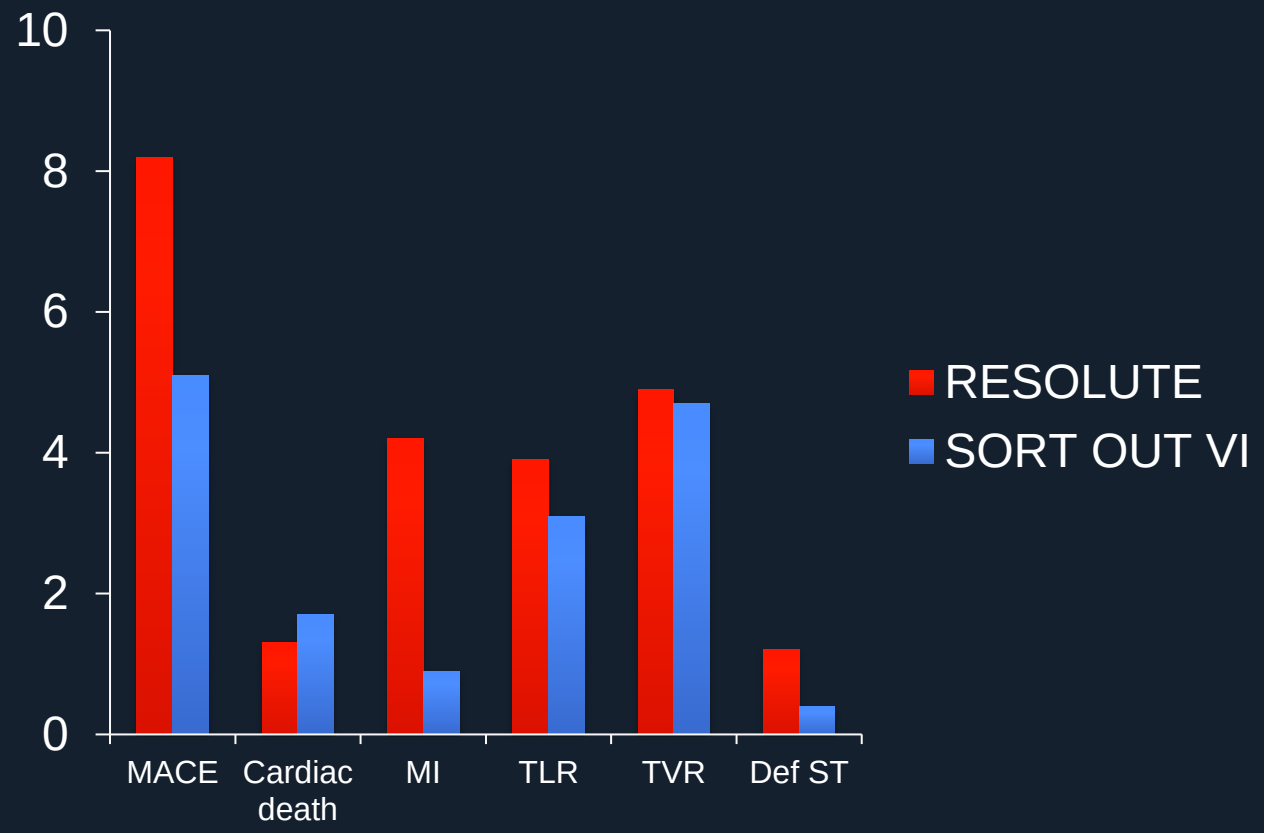
Conclusion

- In the SORT-OUT VI all-comers RCT using patient driven clinical event detection, we found:
- Both the zotarolimus-eluting stents and the biolimus-eluting stents were associated with low major adverse cardiac events.
- The zotarolimus-eluting stent was found to be non-inferior to the biolimus-eluting stent for patients treated with percutaneous coronary intervention.

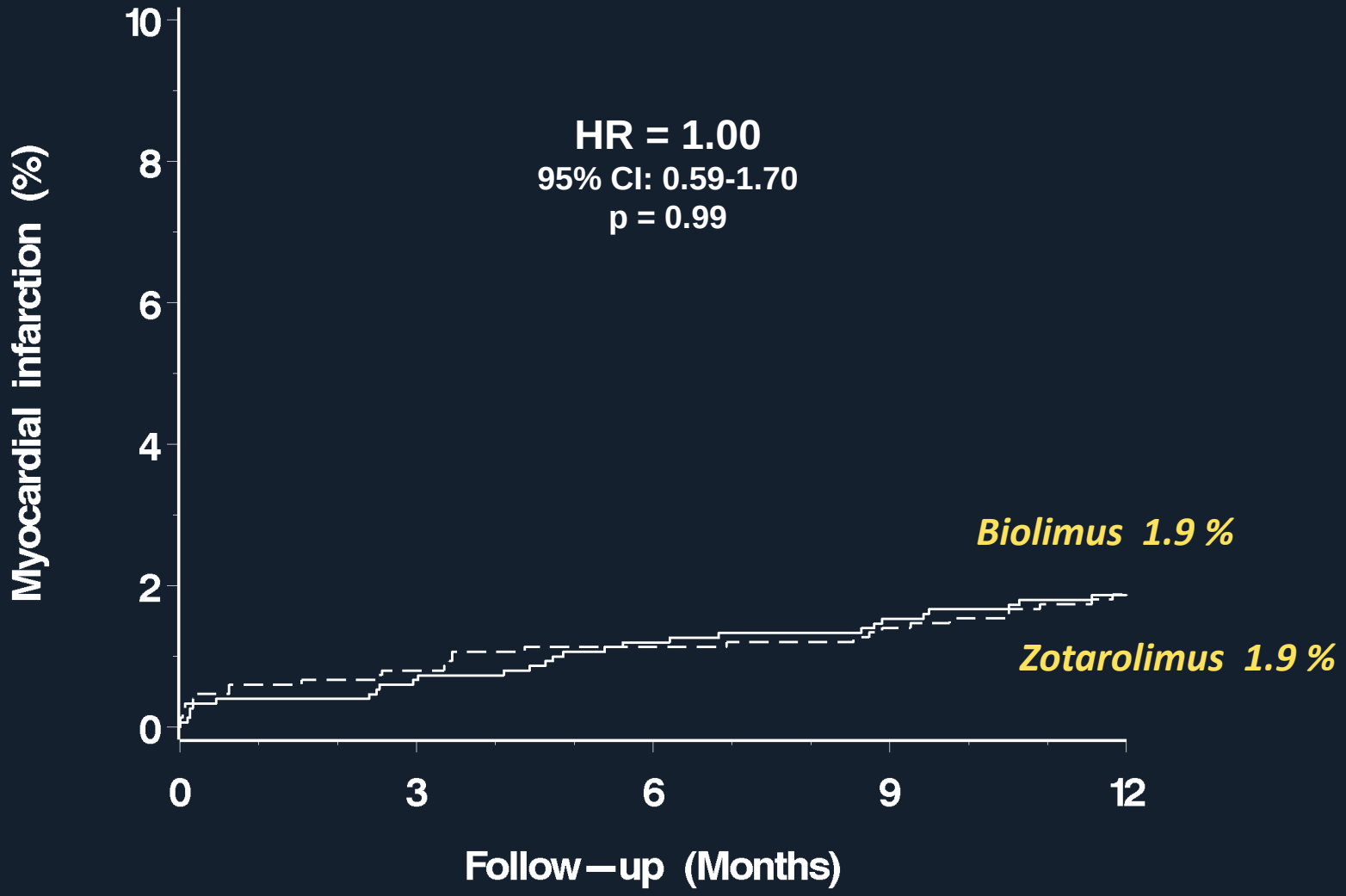
LEADERS vs SORT OUT VI



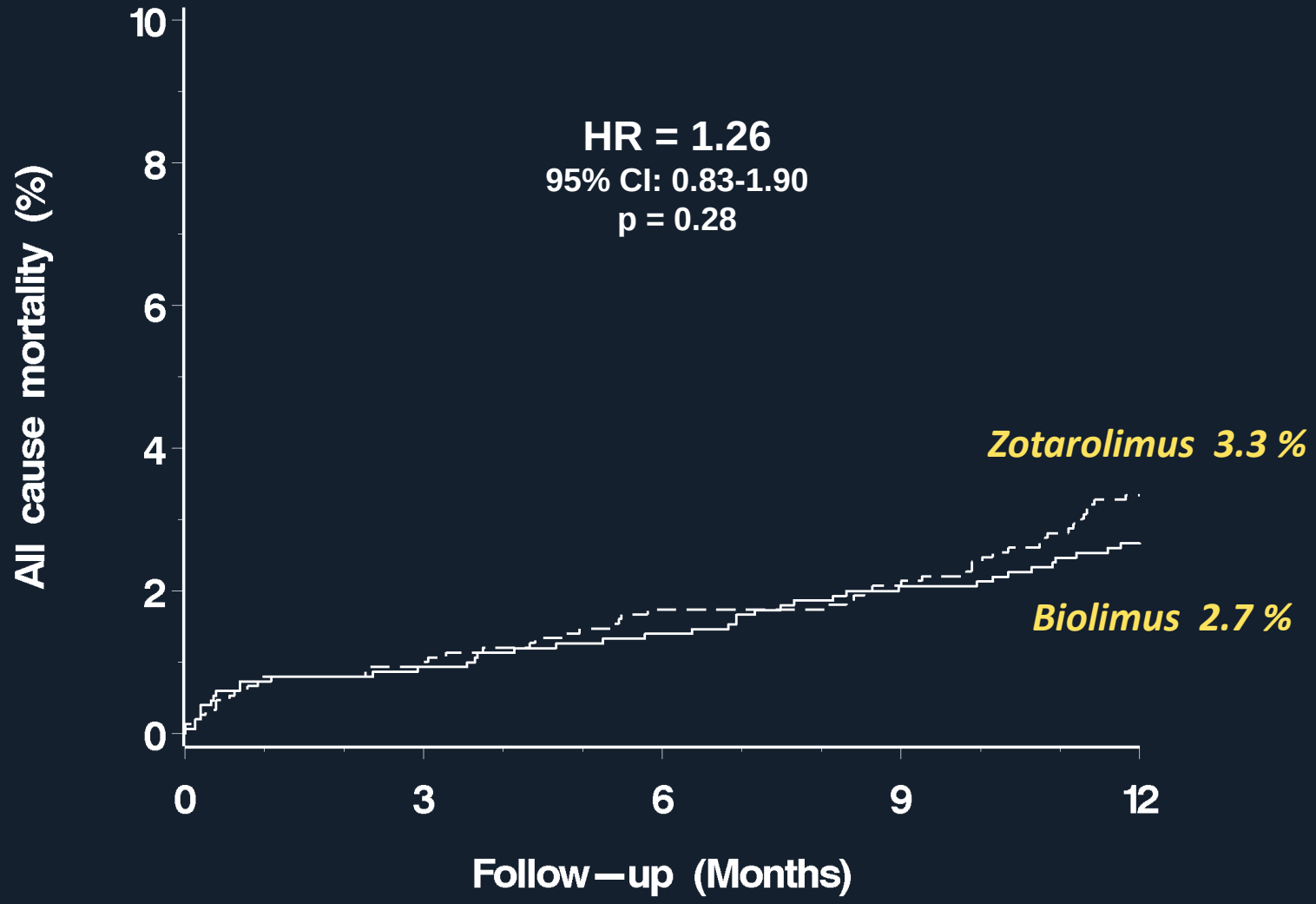
RESOLUTE All Comers vs SORT OUT VI



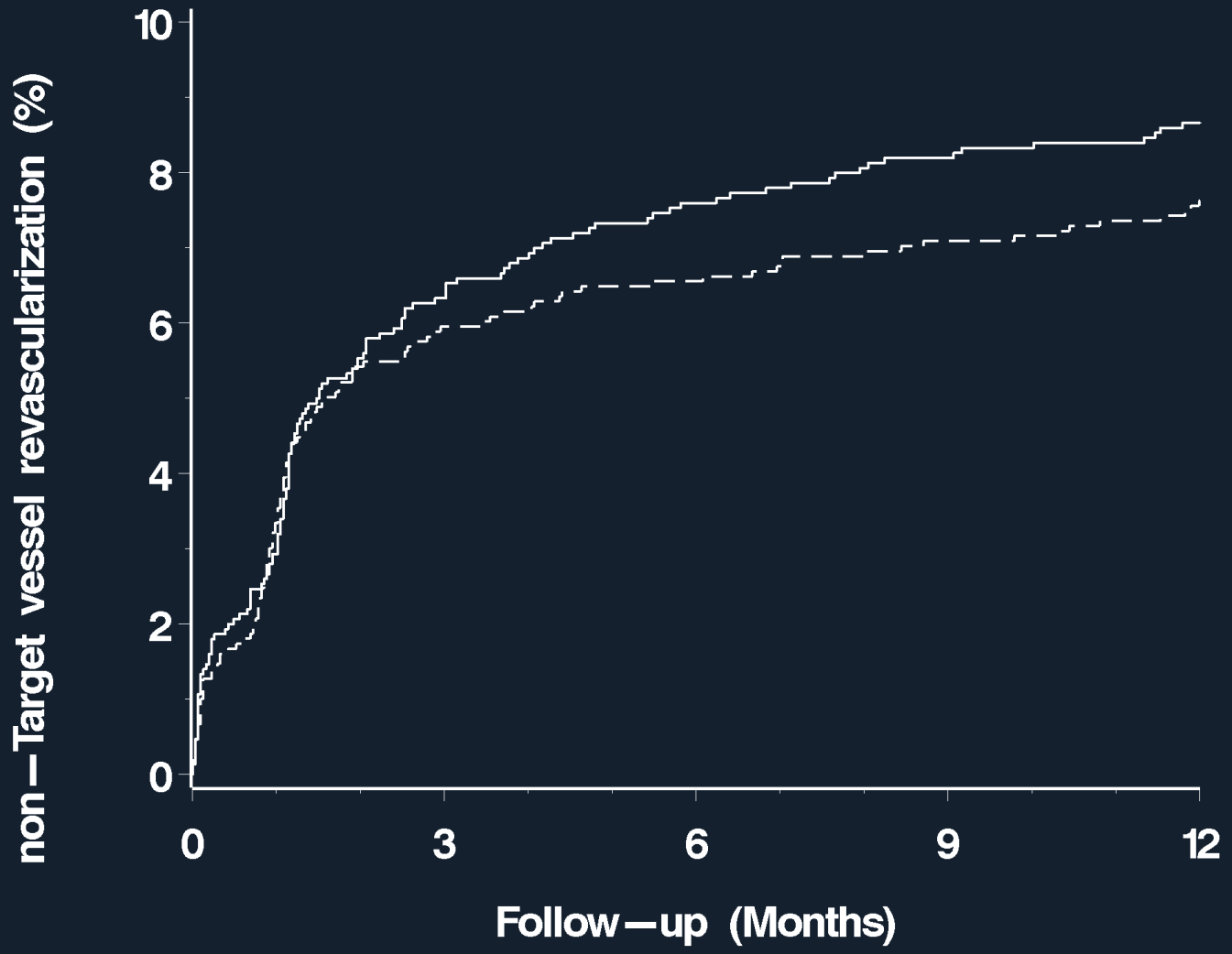
Myocardial Infarction



All Cause Mortality



Non-Target Vessel Revascularization



PCI Organization in Denmark

Population of 5,6 million inhabitants

6 high volume PCI centers

Dual anti-platelet therapy in 12 mo.

Danish Civil Registration System & National Patient Registry, Western Denmark Heart Registry data

- *cause of death*
- *hospital admission diagnosis*
- *diagnosis at discharge*
- *coronary angiography*
- *PCI*
- *CABG*