

# Influence of a biodegradable polymer on long term DES outcomes

From the SORT-OUT Trials

Lisette Okkels Jensen  
Professor DMSci PhD FESC  
Department of Cardiology  
Odense University Hospital  
Odense, Denmark

# Background

- The superior clinical effects of the new generation of DES is a result of the interplay among multiple improvements in stent design including strut thickness, stent geometry, matrix coating, drug concentration, and polymer coating

# Background

- The superior clinical effects of the new generation of DES is a result of the interplay among multiple improvements in stent design including strut thickness, stent geometry, matrix coating, drug concentration, and polymer coating
- Persistence of polymer material on first and second generation drug-eluting stent after completion of drug release has been suggested to be a trigger of a chronic inflammatory response

# Background

- The superior clinical effects of the new generation of DES is a result of the interplay among multiple improvements in stent design including strut thickness, stent geometry, matrix coating, drug concentration, and polymer coating
- Persistence of polymer material on first and second generation drug-eluting stent after completion of drug release has been suggested to be a trigger of a chronic inflammatory response
- Biodegradable polymers may be attractive because they control drug release in the first weeks and then degrade once their function has been served

# Bioabsorbable Polymer in Perspective

## Relative Polymer and Drug Absorption Profiles

**BioMatrix**  
316L-BES



**Nobori**  
316L-BES



**Ultimaster**  
CoCr-SES



**Synergy**  
PtCr-EES



**Orsiro**  
CoCr-SES



**Strut thickness**

120  $\mu\text{m}$

120  $\mu\text{m}$

80  $\mu\text{m}$

74  $\mu\text{m}$

60  $\mu\text{m}$

**Polymer coating**

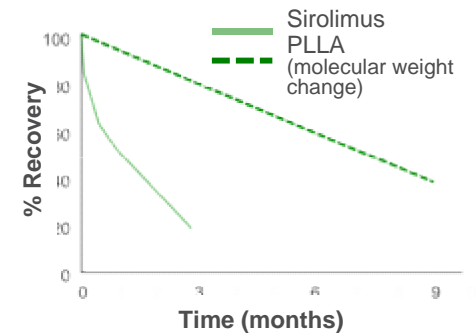
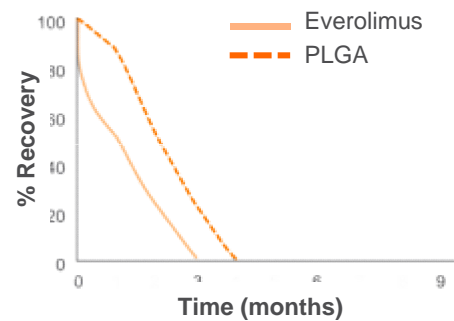
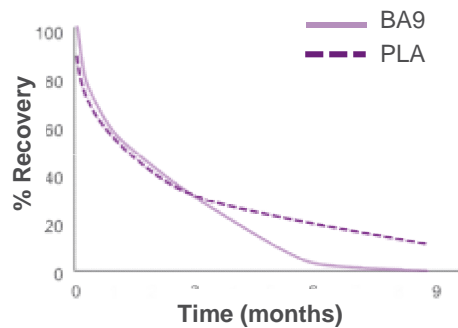
Abluminal  
10  $\mu\text{m}$

Abluminal  
20  $\mu\text{m}$

Abluminal  
15  $\mu\text{m}$

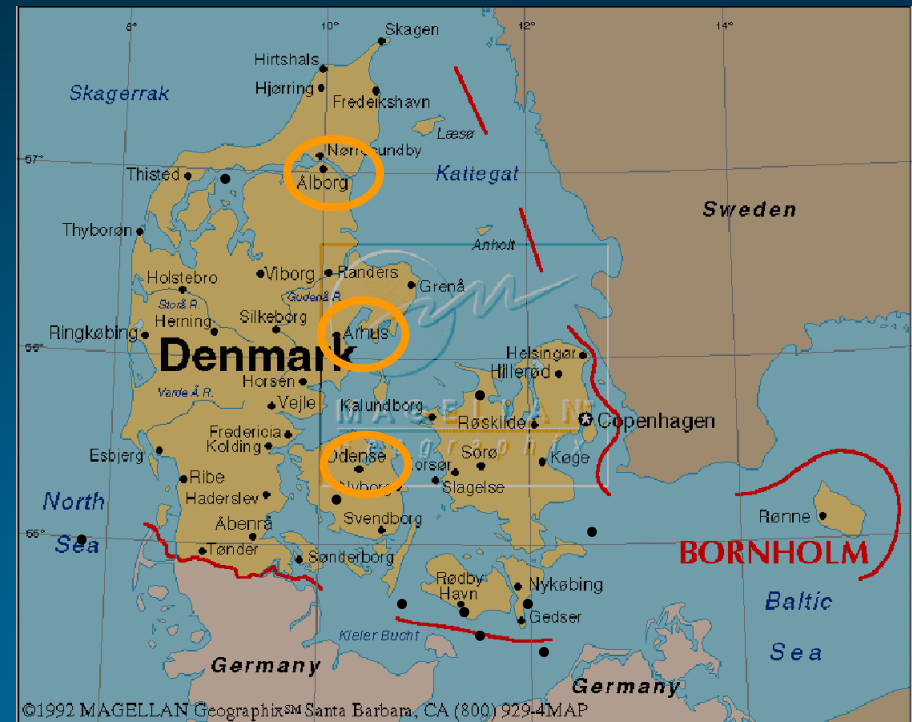
Abluminal  
4  $\mu\text{m}$

Circumferential  
4-7  $\mu\text{m}/\text{side}$



# SORT OUT in DENMARK

- 5.5 million inhabitants in Denmark
- Western Denmark covers 60% of the Danish population
- 3 high-volume 24/7 PCI centers



# SORT-OUT Program

<b>SORT OUT</b>	<b>STENTS</b>	<b>Results (primary endpoint)</b>		<b>Polymer</b>
SORT OUT	BxSonic, Express, Flexmaster			
SORT OUT II	Cypher Taxus	9.3% 11.2%	18M 18M	Durable Polymer Durable Polymer
SORT OUT III	Endeavor Cypher	8.0% 3.9%	12M 12M	Durable Polymer Durable Polymer
SORT OUT IV	Xience V/Promus Cypher Select	4.9% 5.2%	9M 9M	Durable Polymer Durable Polymer
SORT OUT V	Nobori Cypher select	4.1% 3.2%	9M 9M	Bioabsorbable Polymer Durable Polymer
SORT OUT VI	Resolute Biomatrix	5.3% 5.1%	12M 12M	Durable Polymer Bioabsorbable Polymer
SORT OUT VII	Orsiro Nobori	3.8% 4.6%	12M 12M	Bioabsorbable Polymer Bioabsorbable Polymer
SORT OUT VIII	Synergy Biomatrix	Enrolment completed		Bioabsorbable Polymer Bioabsorbable Polymer
SORT OUT IX	BioFreedom Orsiro	Ongoing		No Polymer Bioabsorbable Polymer

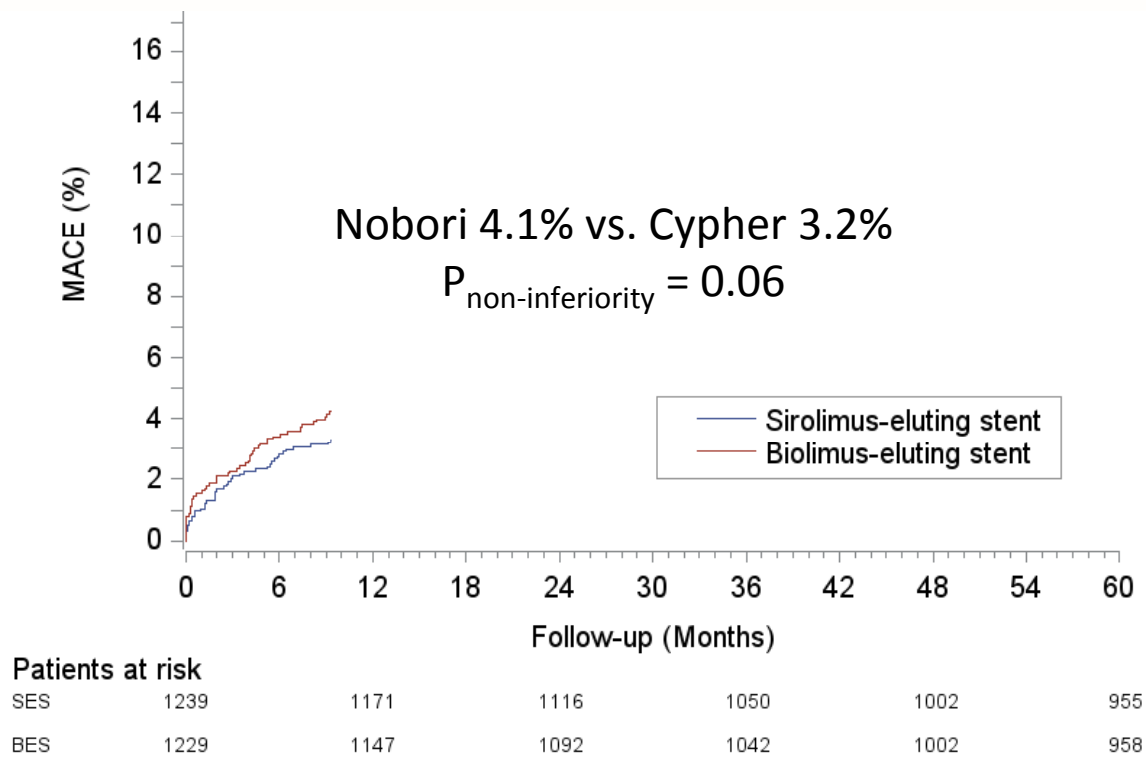
# SORT-OUT Program

SORT OUT	STENTS	Results (primary endpoint)		Polymer
SORT OUT	BxSonic, Express, Flexmaster			
SORT OUT II	Cypher Taxus	9.3% 11.2%	18M 18M	Durable Polymer Durable Polymer
SORT OUT III	Endeavor Cypher	8.0% 3.9%	12M 12M	Durable Polymer Durable Polymer
SORT OUT IV	Xience V/Promus Cypher Select	4.9% 5.2%	9M 9M	Durable Polymer Durable Polymer
SORT OUT V	<b>Nobori</b> Cypher select	4.1% 3.2%	9M 9M	<b>Bioabsorbable Polymer</b> Durable Polymer
SORT OUT VI	Resolute <b>Biomatrix</b>	5.3% 5.1%	12M 12M	Durable Polymer <b>Bioabsorbable Polymer</b>
SORT OUT VII	<b>Orsiro</b> <b>Nobori</b>	3.8% 4.6%	12M 12M	<b>Bioabsorbable Polymer</b> <b>Bioabsorbable Polymer</b>
SORT OUT VIII	<b>Synergy</b> <b>Biomatrix</b>	Enrolment completed		<b>Bioabsorbable Polymer</b> <b>Bioabsorbable Polymer</b>
SORT OUT IX	BioFreedom <b>Orsiro</b>	Ongoing		No Polymer <b>Bioabsorbable Polymer</b>



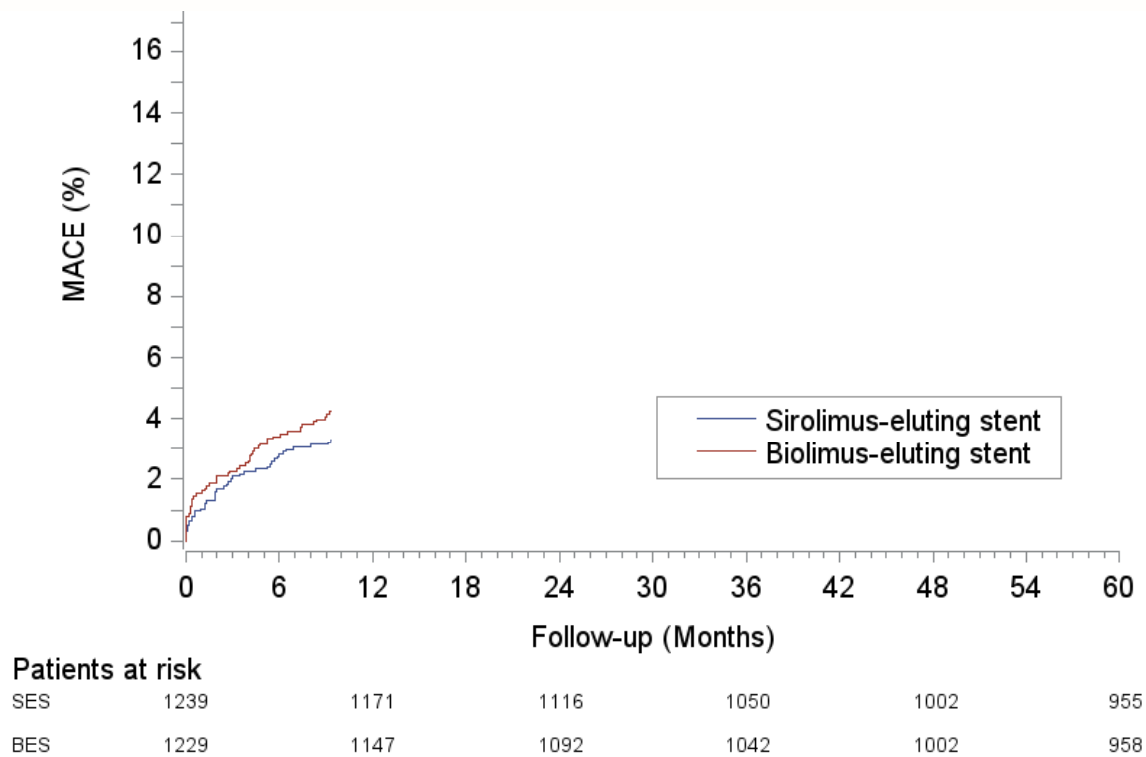
# 1<sup>o</sup> Endpoint: Major Adverse Cardiac Events

(Cardiac death, myocardial infarction, definite stent thrombosis, target vessel revascularization)



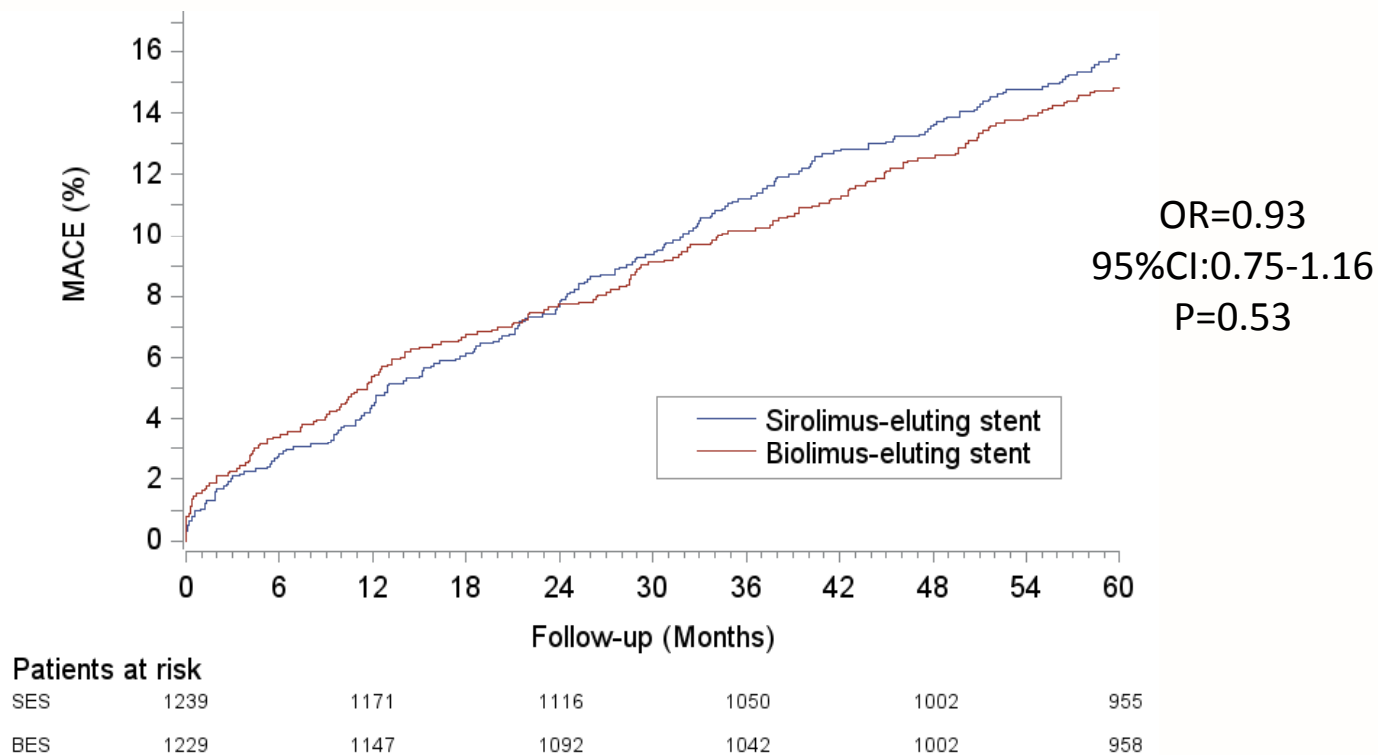
# 5Y Endpoint: Major Adverse Cardiac Events

(Cardiac death, myocardial infarction, definite stent thrombosis, target vessel revascularization)

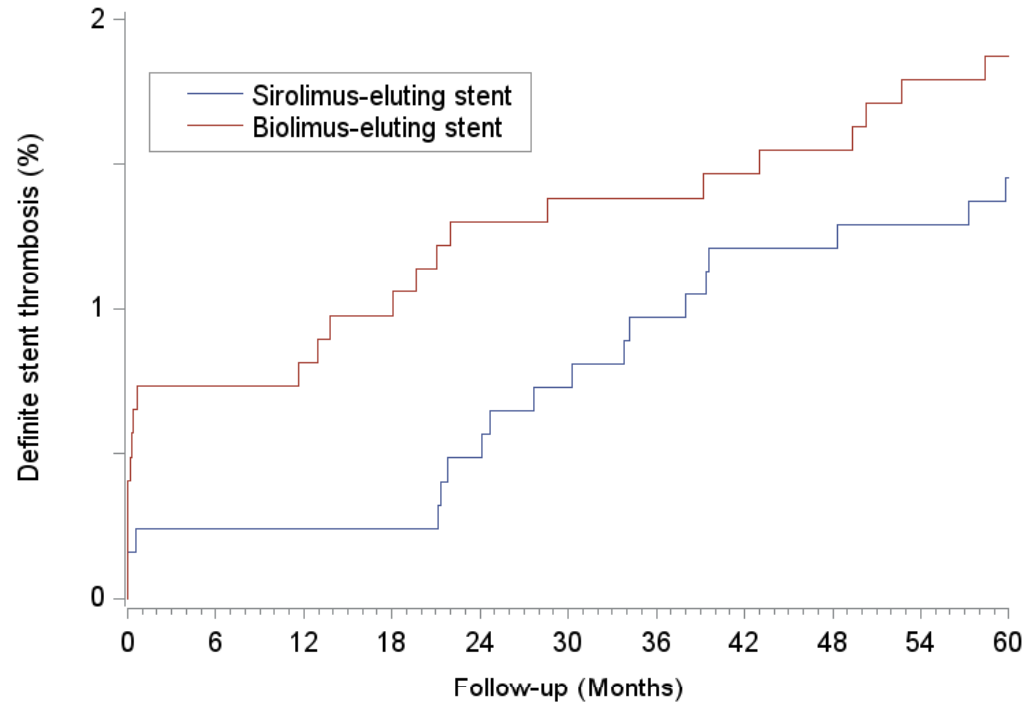


# 5Y Endpoint: Major Adverse Cardiac Events

(Cardiac death, myocardial infarction, definite stent thrombosis, target vessel revascularization)



# 5 year: Definite Stent thrombosis



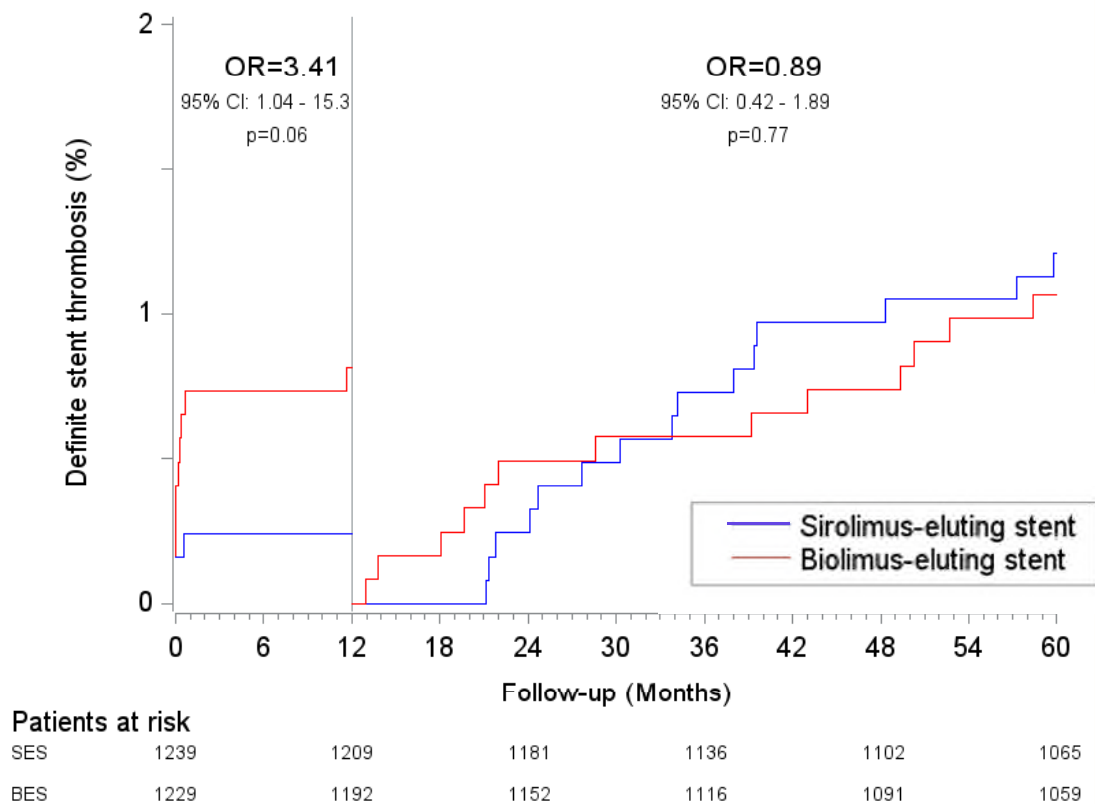
OR=1.31  
 95%CI:0.70-2.47  
 P=0.40

### Patients at risk

	0	6	12	18	24	30	36	42	48	54	60
SES	1239	1209	1181	1136	1102	1065					
BES	1229	1192	1152	1116	1091	1059					



## Landmark analysis discriminating between definite stent thrombosis occurring before and after 1 year



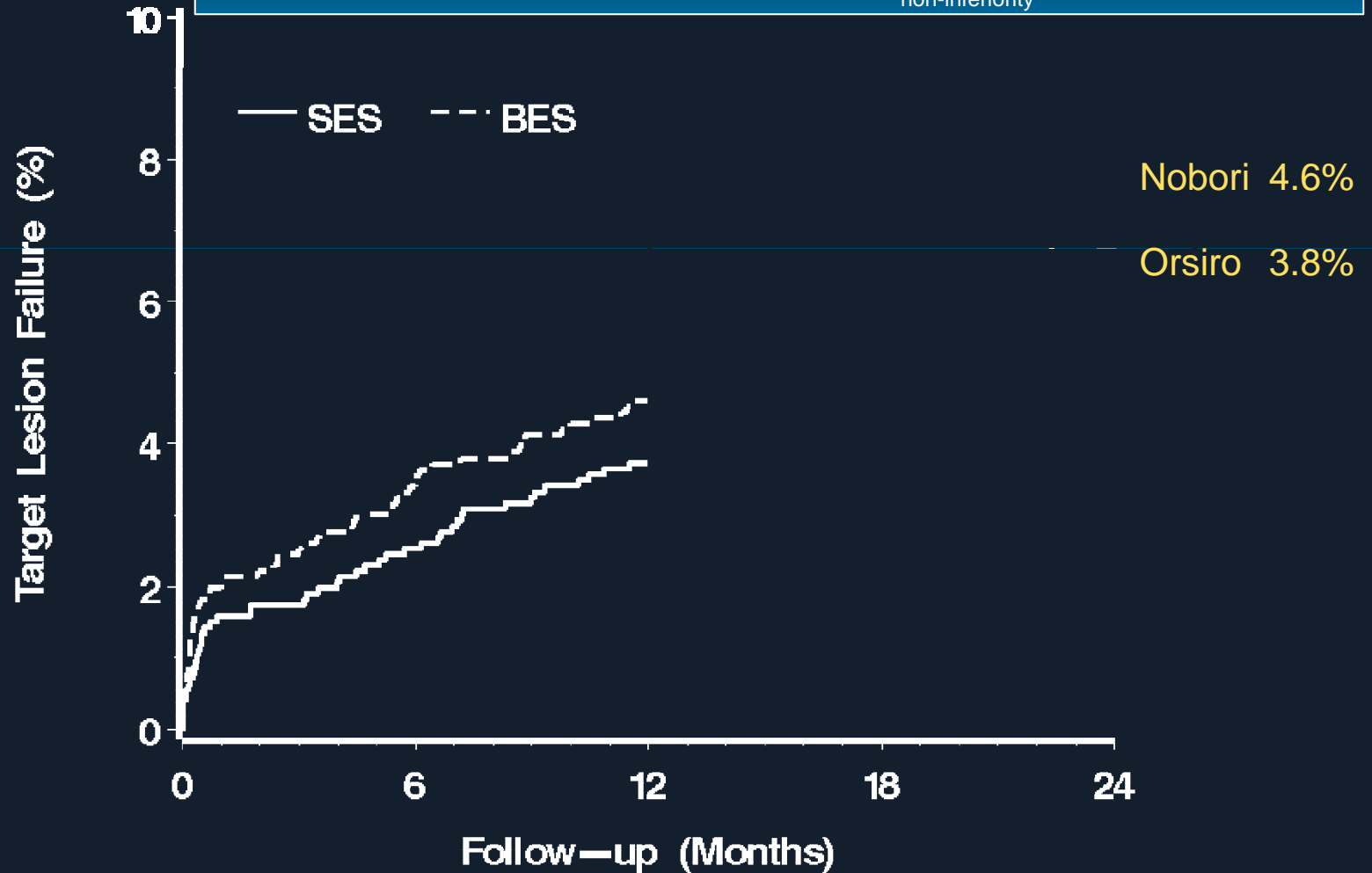
# Randomized comparison of a sirolimus-eluting stent with a biolimus-eluting stent in patients treated with PCI: the SORT OUT VII trial

Lisette Okkels Jensen, Per Thayssen, Michael Maeng, Jan Ravkilde, Lars Krusell, Hans-Henrik Tilsted, Anders Junker, Christian Juhl Terkelsen, Karsten Tange Veien, Anne Kaltoft, Anton Boel Villadsen, Jens Aaroe, Klára Berencsi, Svend Eggert Jensen, Knud Nørregaard Hansen, Steen Dalby Kristensen, Morten Madsen, Hans Erik Bøtker, Henrik Steen Hansen, Bent Raungaard, Jens Flensted Lassen, Evald Høj Christiansen

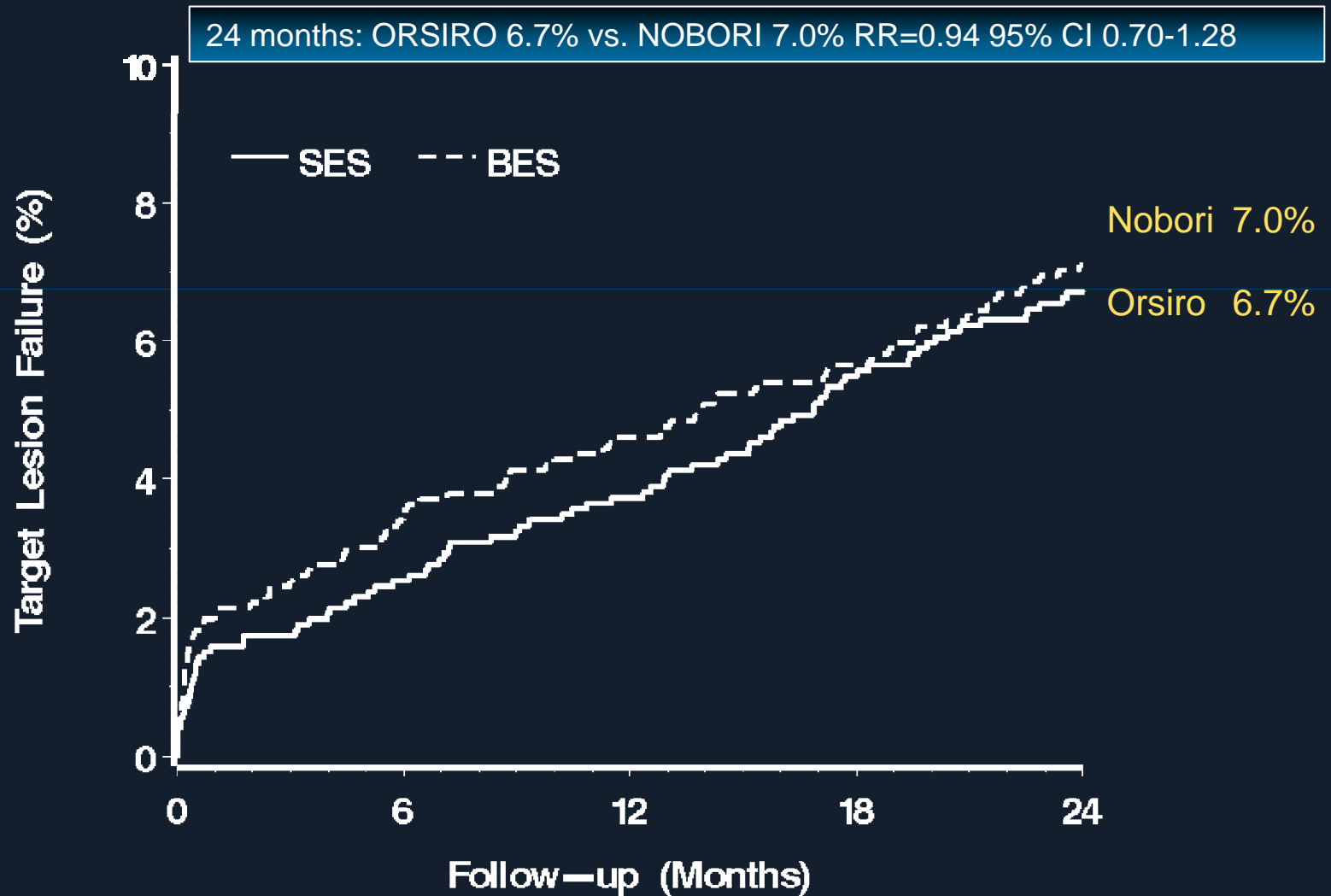
*Odense University Hospital, Aarhus University Hospital, Aalborg University Hospital - DENMARK*

# SO VII: Target Lesion Failure

12 months: ORSIRO 3.8% vs. NOBORI 4.6%  $P_{\text{non-inferiority}} < 0.0001$



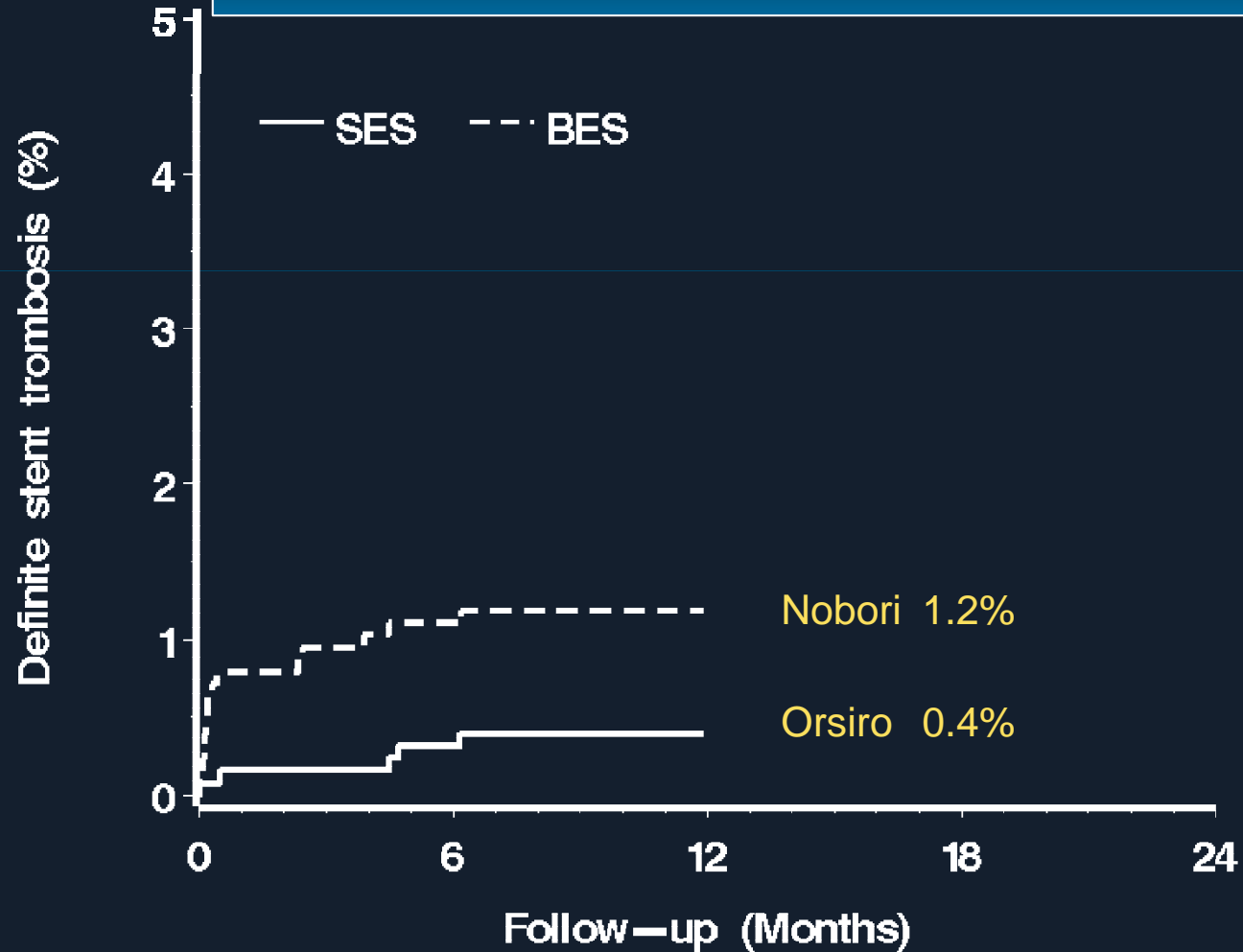
# SO VII: Target Lesion Failure





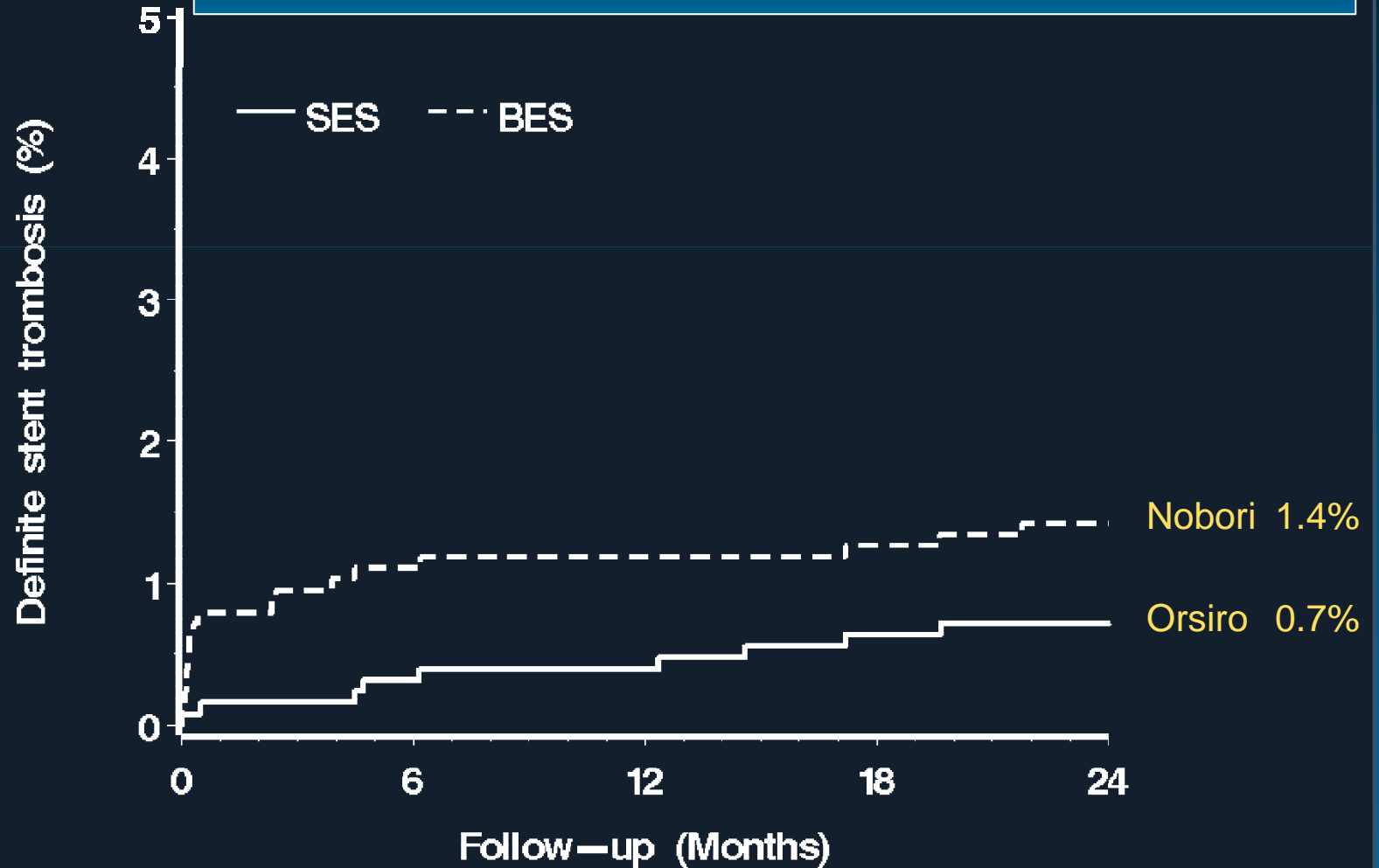
# SO VII: Definite Stent Thrombosis

24 months: ORSIRO 0.4% vs. NOBORI 1.2% RR=0.33 95% CI 0.12-0.92

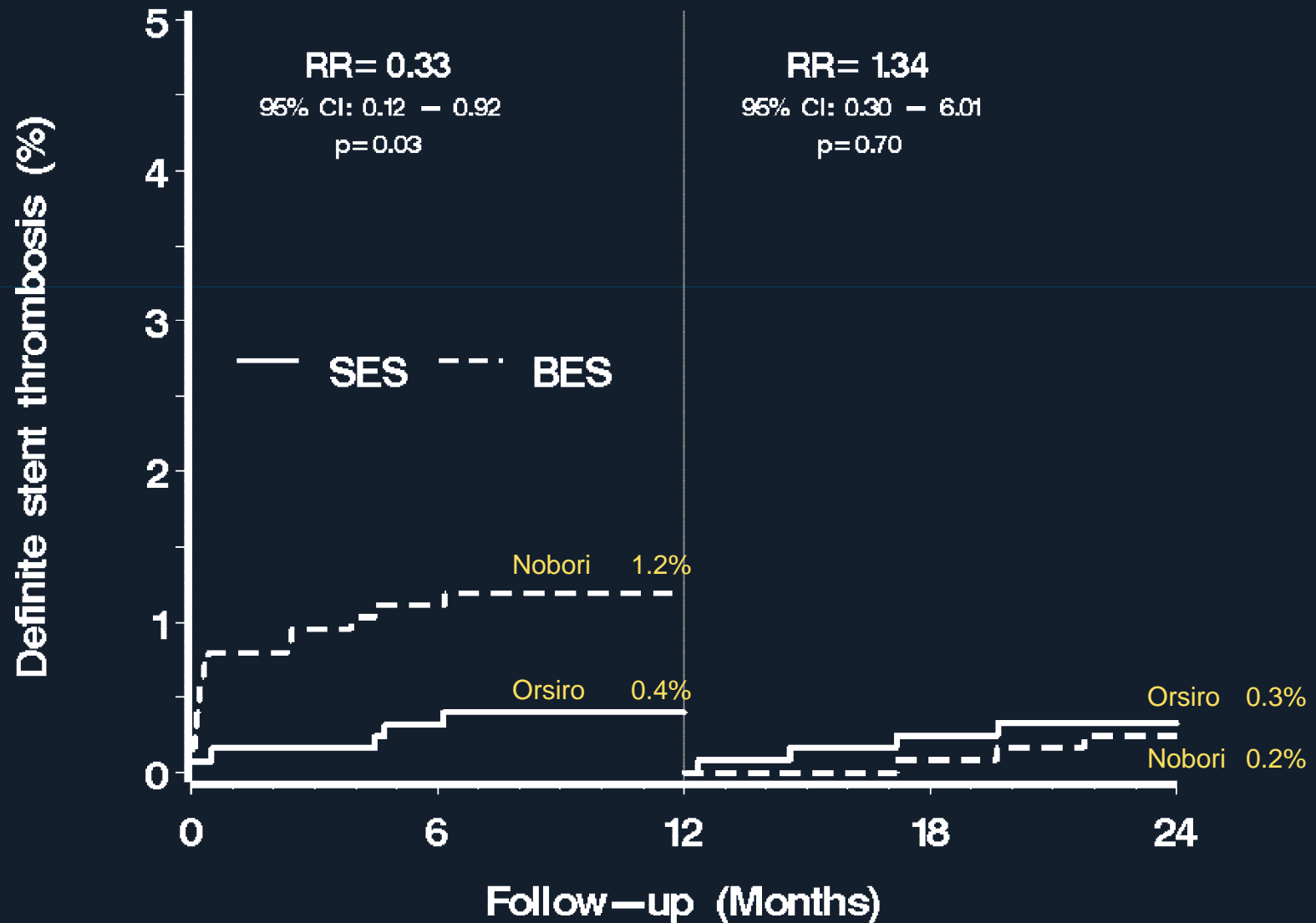


# SO VII: Definite Stent Thrombosis

24 months: ORSIRO 0.7% vs. NOBORI 1.4% RR=0.50 95% CI 0.23-1.12

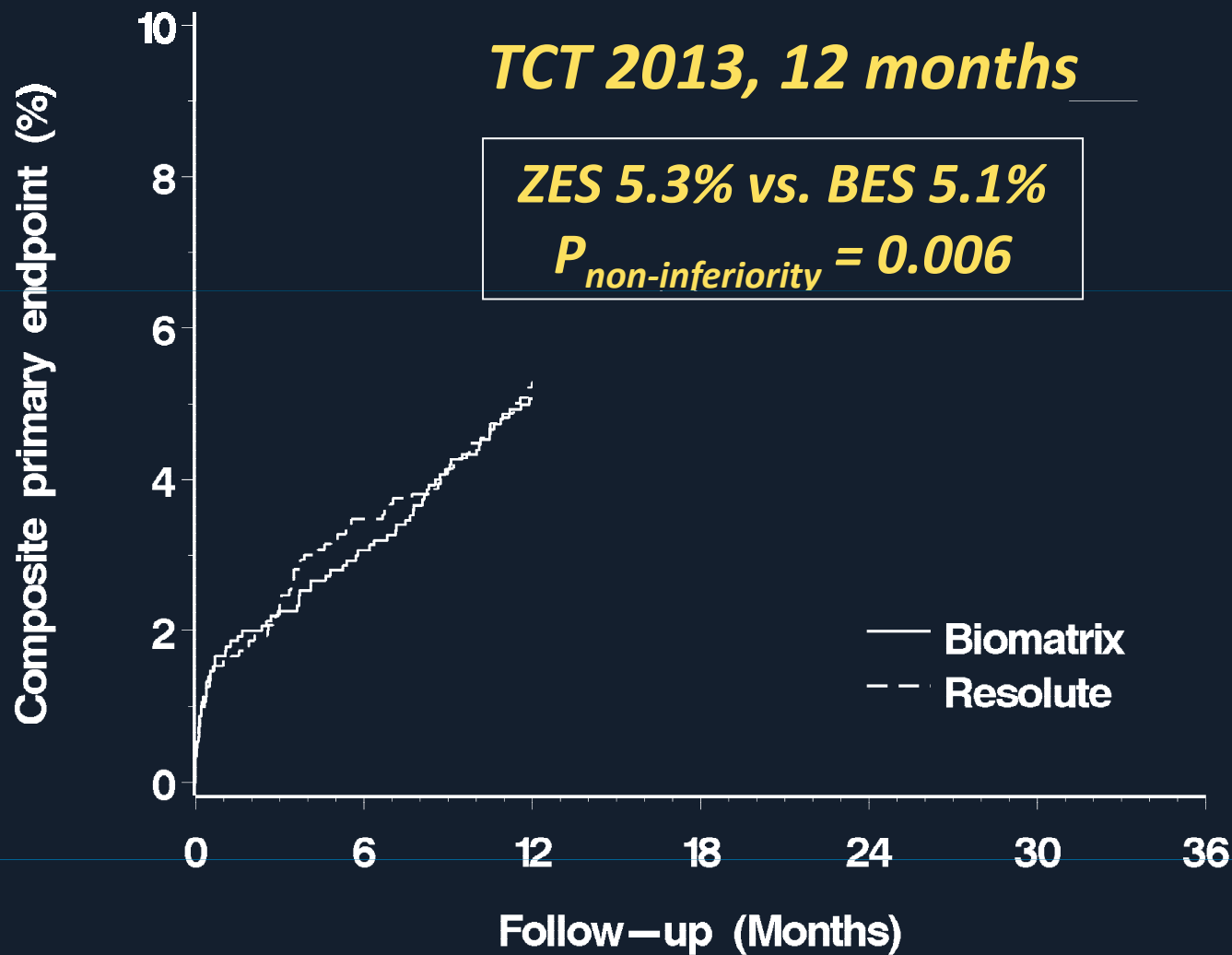


# SO VII: Definite Stent Thrombosis



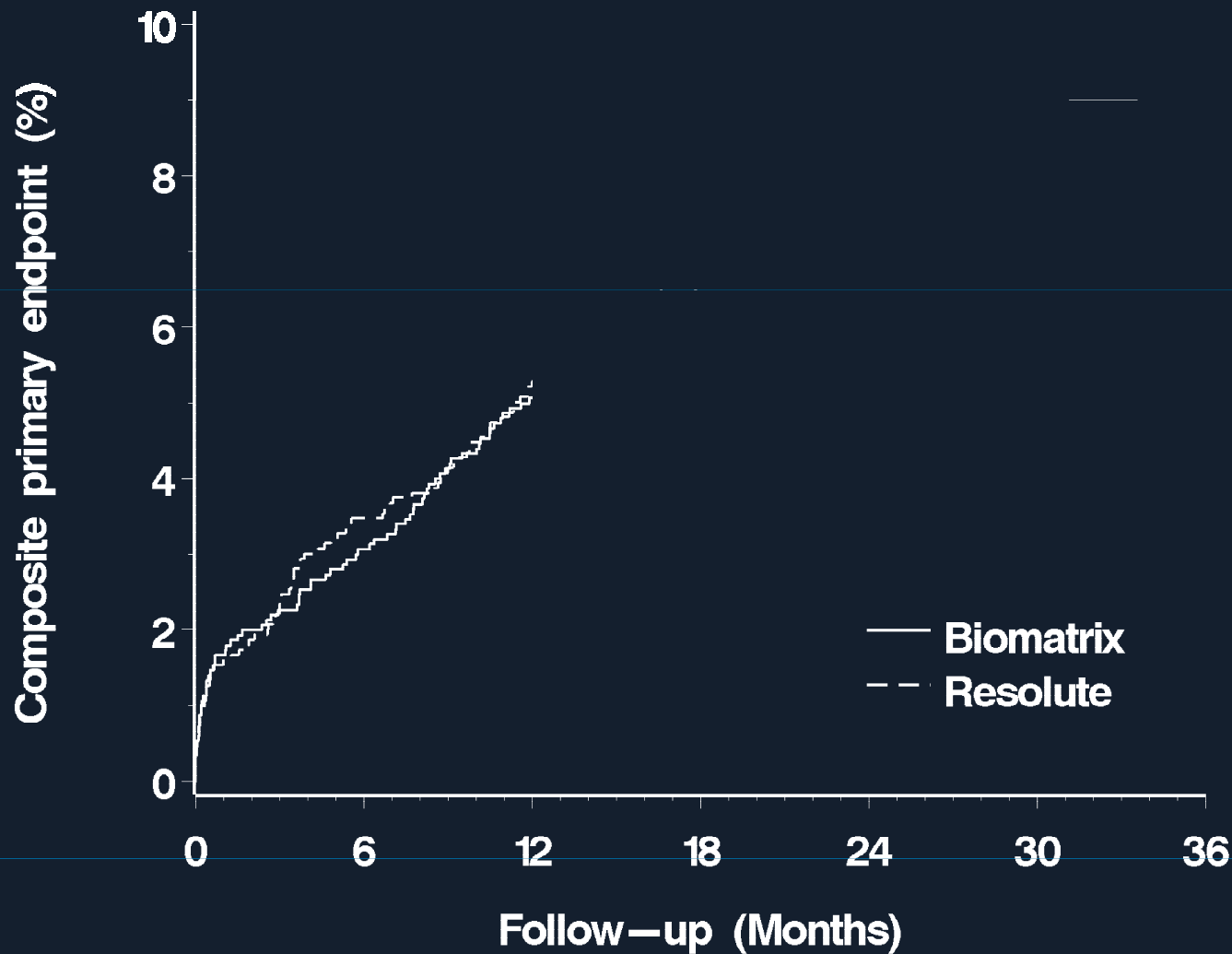
# SO VI: Major Adverse Cardiac Events

(Cardiac death, myocardial infarction, target lesion revascularization)



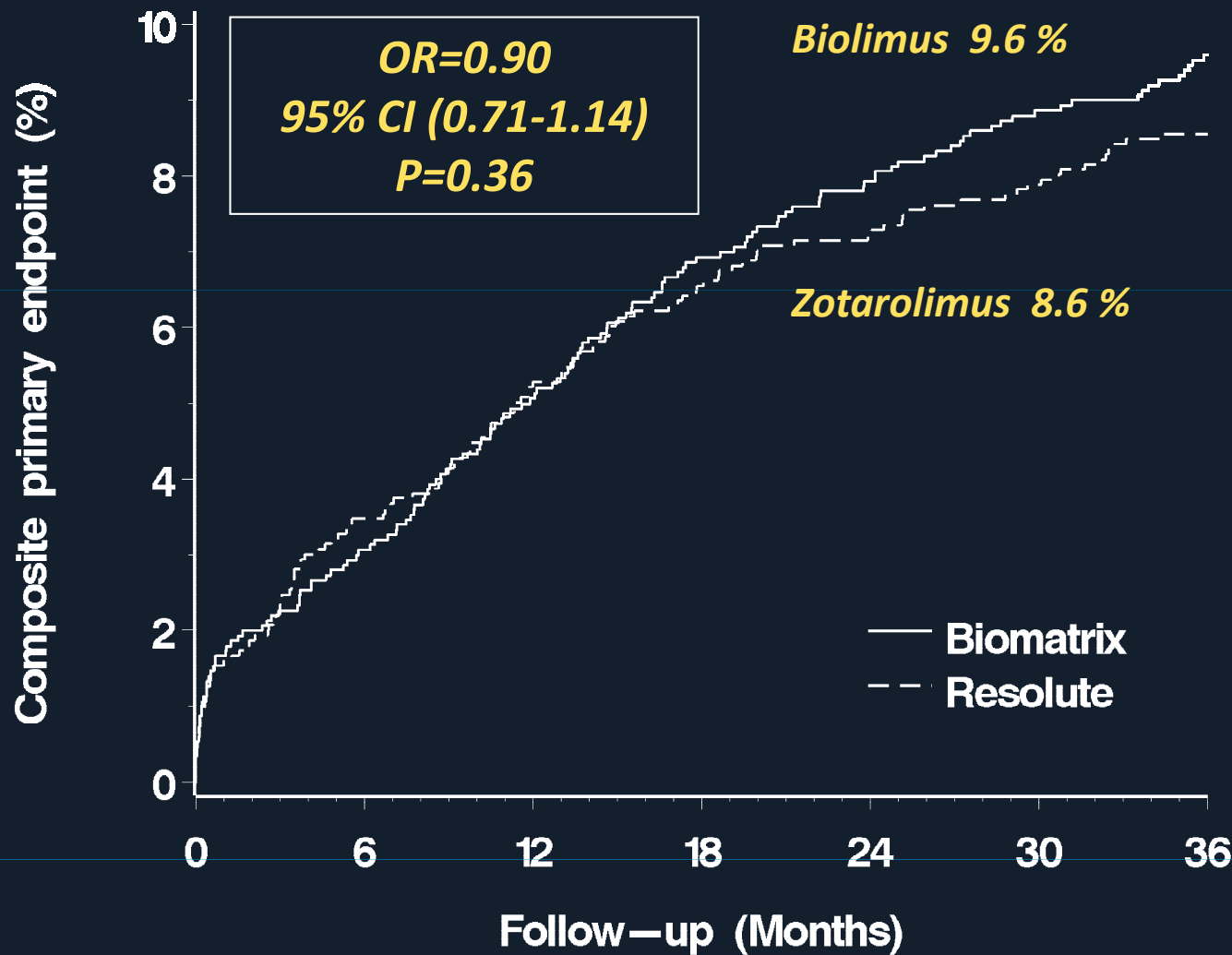
# SO VI: Major Adverse Cardiac Events

(Cardiac death, myocardial infarction, target lesion revascularization)

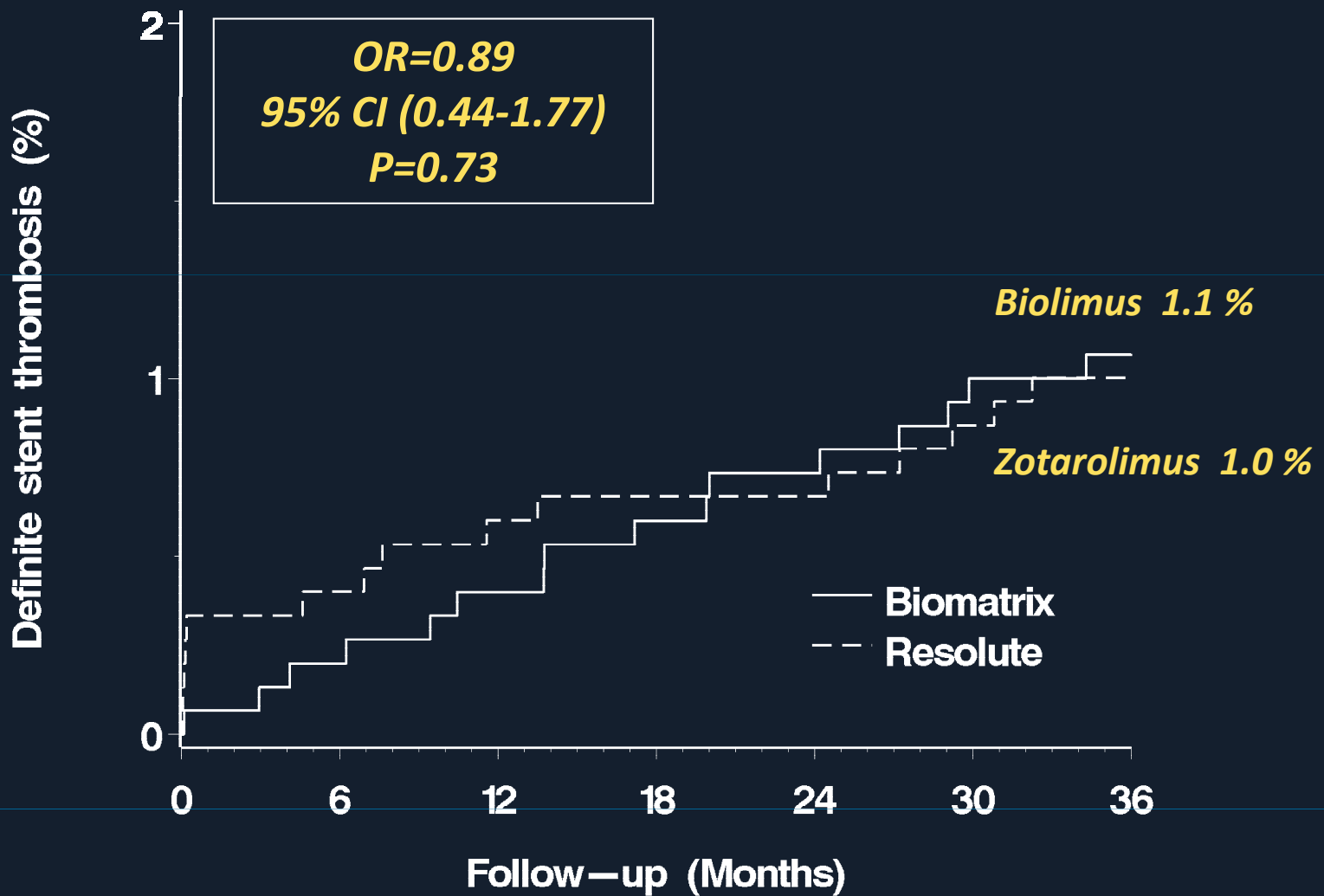


# SO VI: Major Adverse Cardiac Events

(Cardiac death, myocardial infarction, target lesion revascularization)



# SO VI Stent Thrombosis



# Pooled data from SORT OUT III-VI

Patients (n=10,410)

- **SORT OUT III**  
Cypher sirolimus-eluting vs. Endeavor zotarolimus-eluting stents
- **SORT OUT IV**  
Cypher sirolimus-eluting vs. Xience everolimus-eluting stents
- **SORT OUT V**  
Cypher sirolimus-eluting vs. Nobori biolimus-eluting stents
- **SORT OUT VI**  
Resolute zotarolimus-eluting vs. Biomatrix biolimus-eluting stents



# Pooled data from SORT OUT III-VI

Patients (n=10,410)

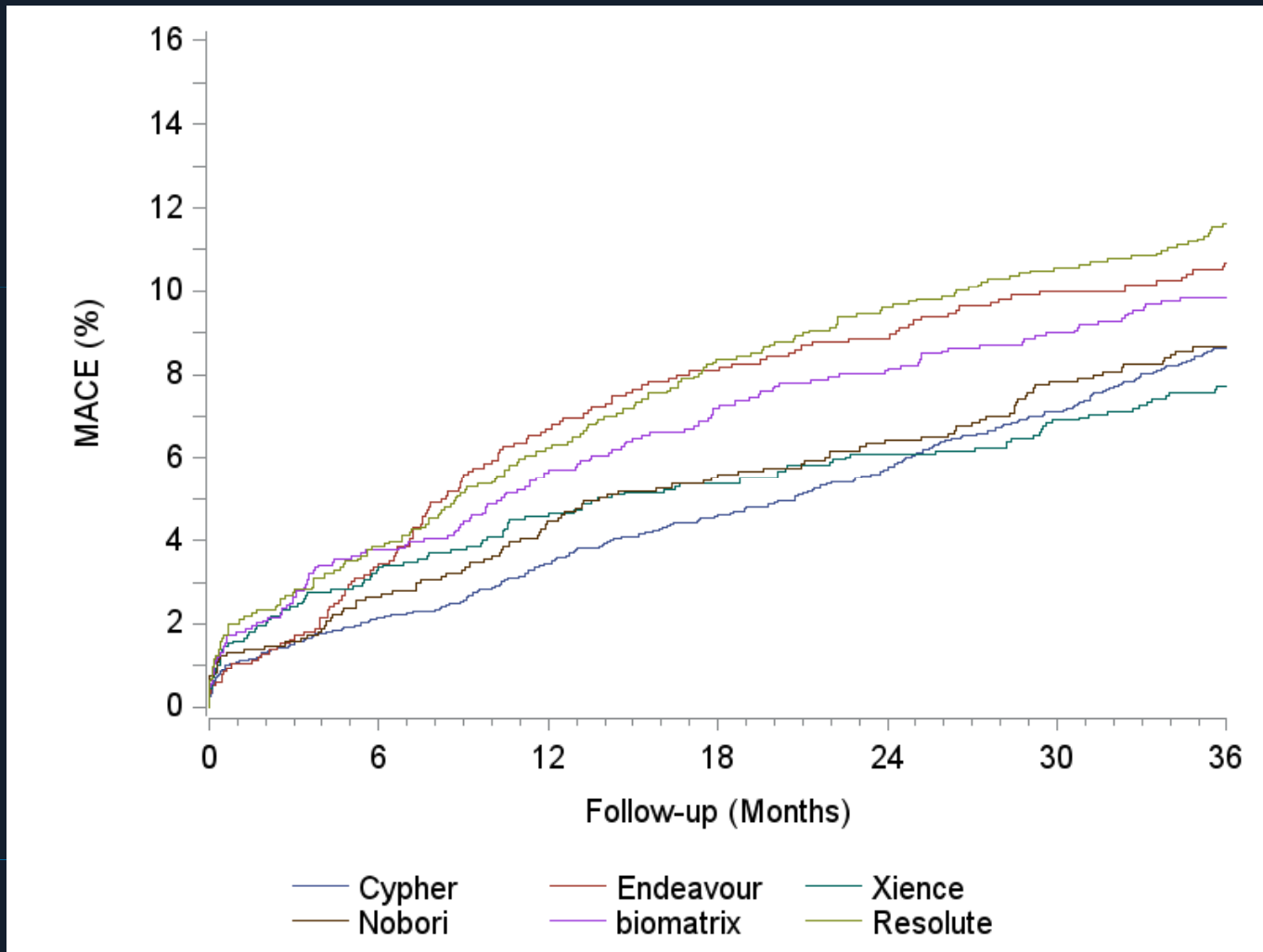
3-year outcomes in patients treated with the first generation sirolimus-eluting Cypher stent, second generation zotarolimus-eluting or everolimus-eluting; or biodegradable polymer biolimus-eluting Nobori / Biomatrix stents

**MACE:** Cardiac death, myocardial infarction, target lesion revascularization

- Cypher sirolimus-eluting (n=3,764 patients)
- Endeavor zotarolimus-eluting (n=1,162)
- Resolute zotarolimus-eluting (n=1,458)
- Xience V/Promus everolimus-eluting stents (n=1,376)
- Nobori / Biomatrix biolimus-eluting (n=2,650 patients)

# Pooled data from SORT OUT III-VI

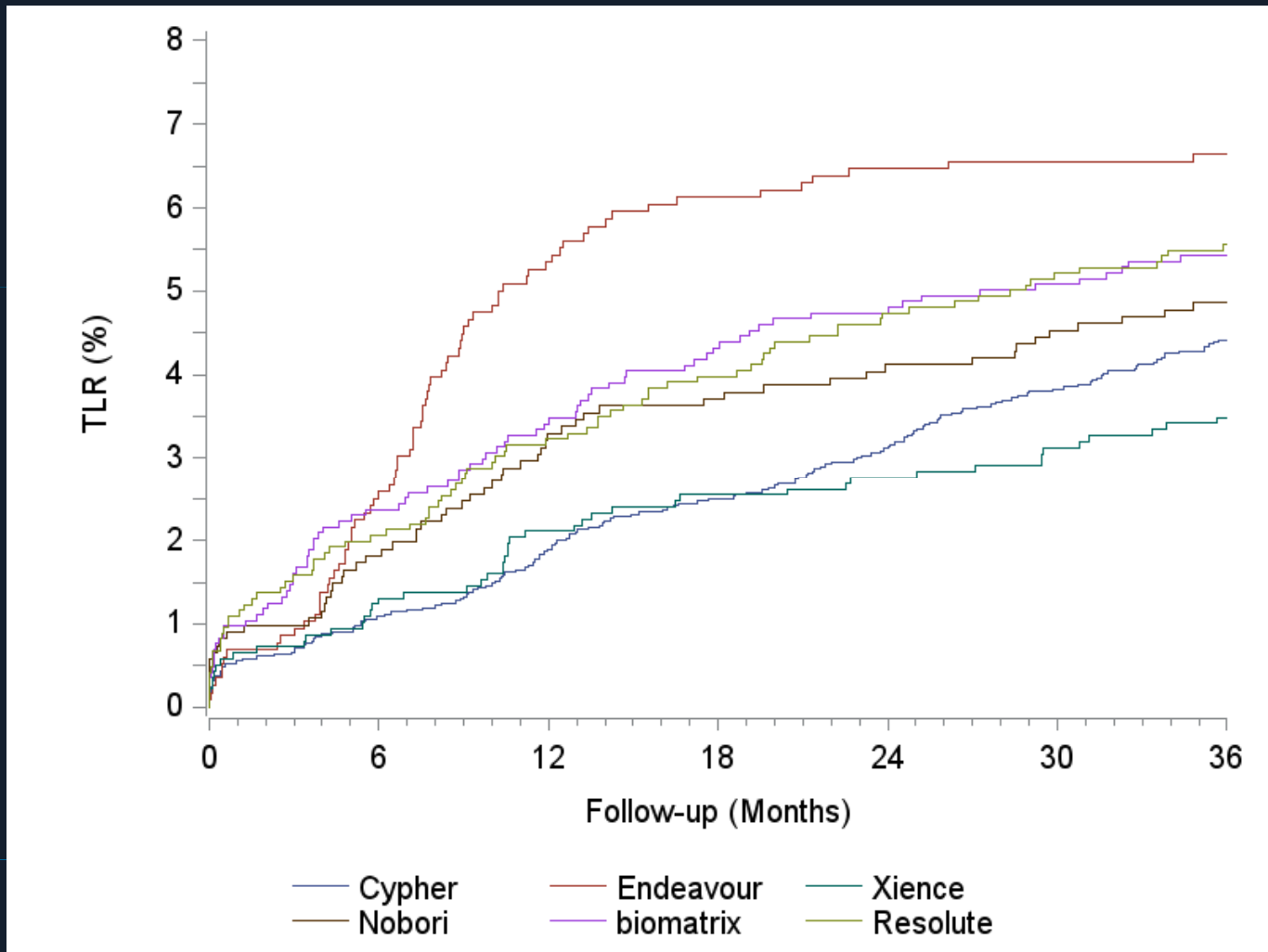
Patients (n=10,410)



Resolute  
Endeavor  
Biomatrix  
Nobori  
Cypher  
Xience

# Pooled data from SORT OUT III-VI

Patients (n=10,410)

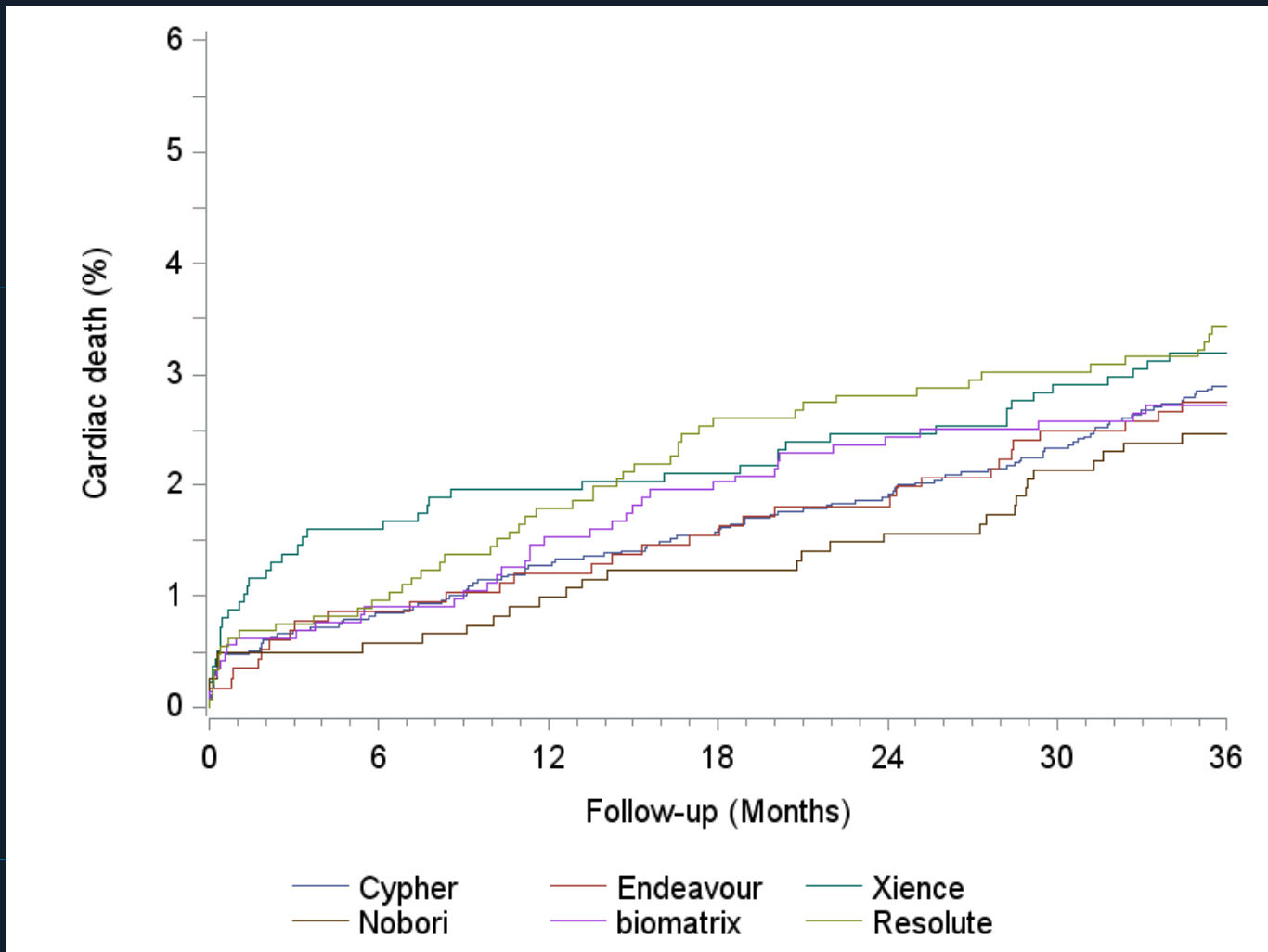


Endeavour  
Resolute  
Biomatrix  
Nobori  
Cypher  
Xience

— Cypher — Endeavour — Xience  
— Nobori — biomatrix — Resolute

# Pooled data from SORT OUT III-VI

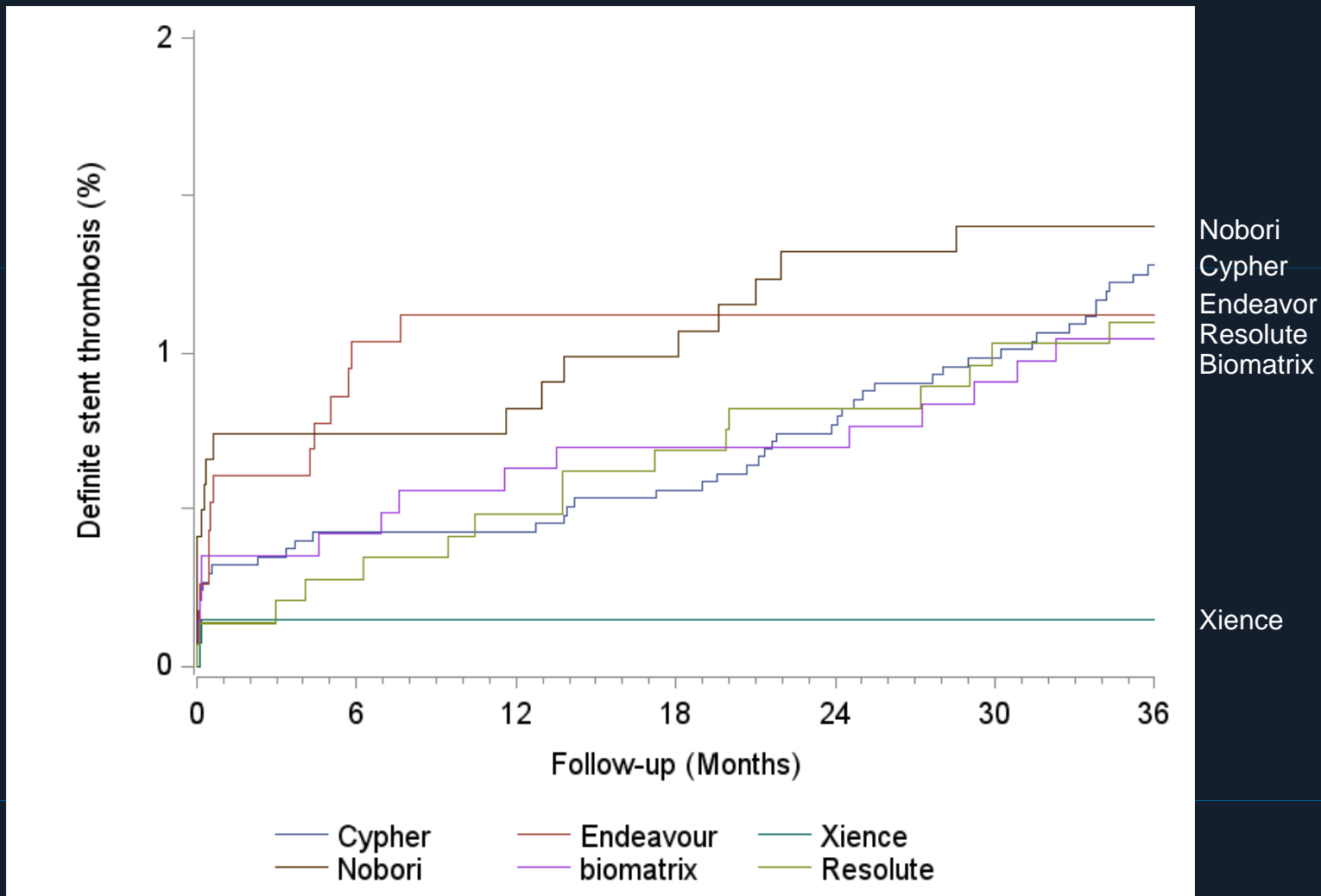
Patients (n=10,410)



Resolute  
Xience  
Cypher  
Endeavour  
Biomatrix  
Nobori

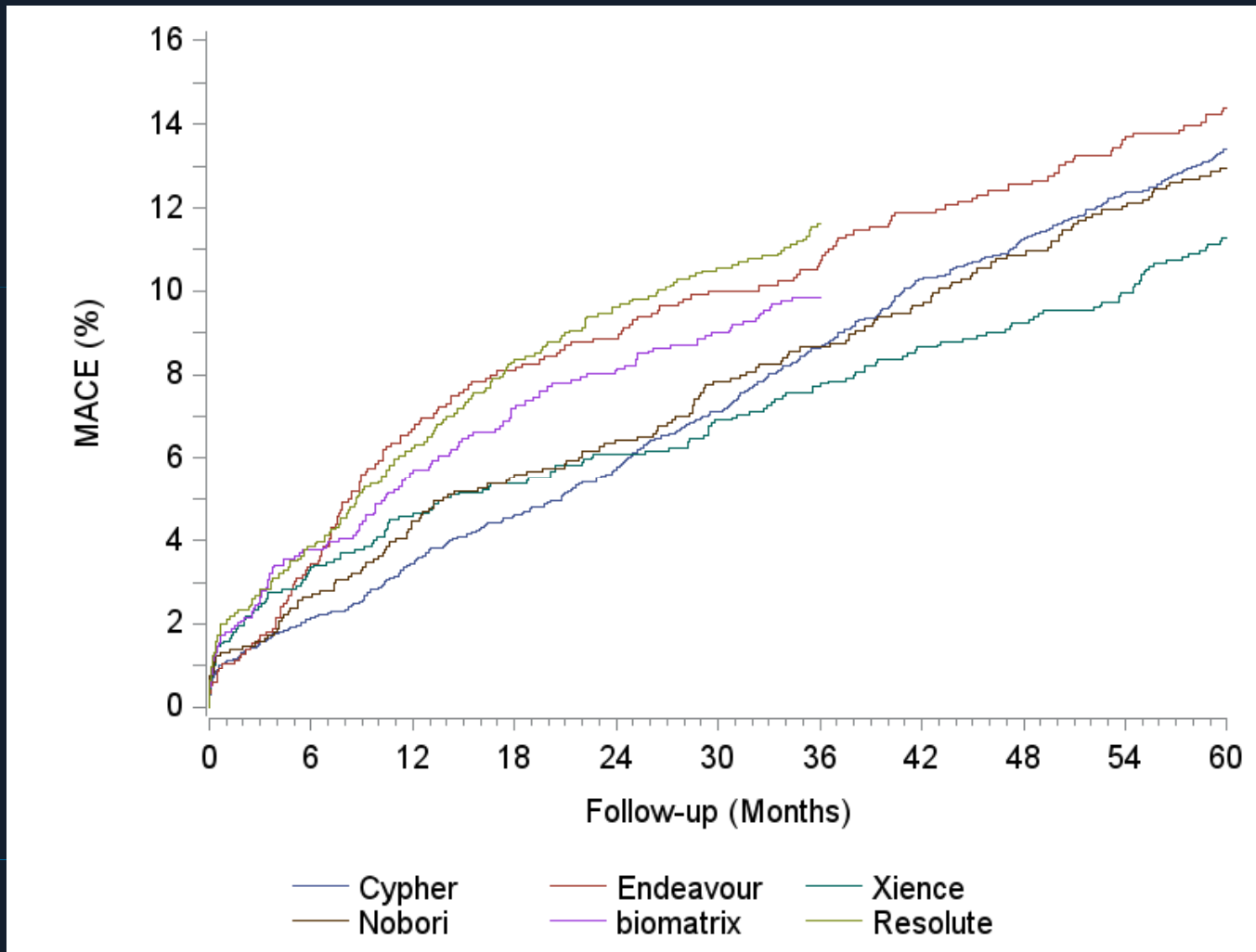
# Pooled data from SORT OUT III-VI

Patients (n=10,410)



# Pooled data from SORT OUT III-VI

Patients (n=10,410)

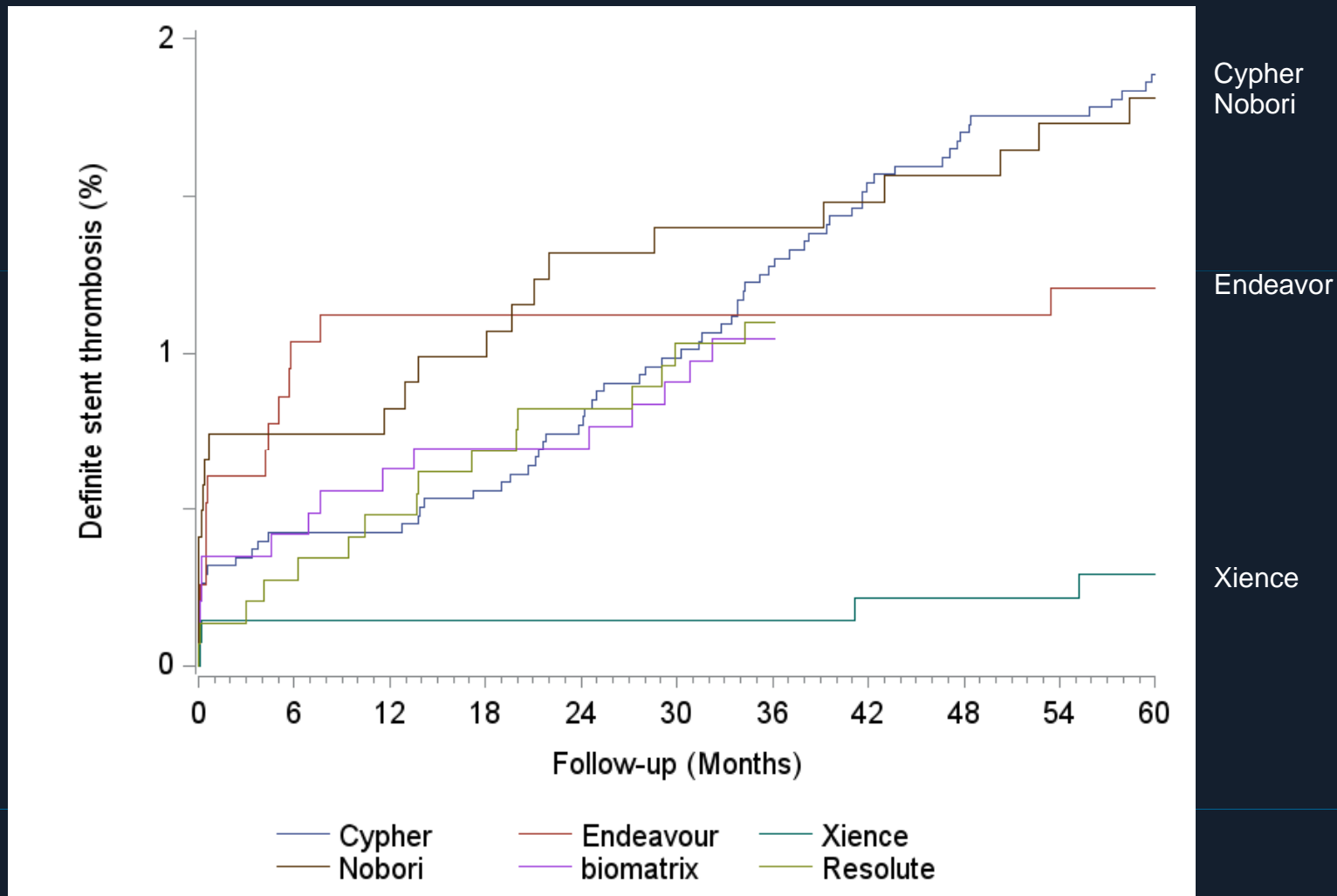


Endeavor  
Cypher  
Nobori  
Xience

Cypher Endeavour Xience  
Nobori biomatrix Resolute

# Pooled data from SORT OUT III-VI

Patients (n=10,410)



# Conclusion

- In comparison to the first-generation Cypher sirolimus-eluting stent, none of the evaluated newer-generation drug-eluting stents reduced stent-related adverse outcomes at 3-year follow-up



# Conclusion

- In comparison to the first-generation Cypher sirolimus-eluting stent, none of the evaluated newer-generation drug-eluting stents reduced stent-related adverse outcomes at 3-year follow-up
- Xience everolimus-eluting stent, however, was associated with a major reduction of definite stent thrombosis

# Conclusion

- In comparison to the first-generation Cypher sirolimus-eluting stent, none of the evaluated newer-generation drug-eluting stents reduced stent-related adverse outcomes at 3-year follow-up
- Xience everolimus-eluting stent, however, was associated with a major reduction of definite stent thrombosis
- Biodegradable polymer biolimus-eluting stents did not improve target lesion failure or risk of very late stent thrombosis compared to first generation Cypher sirolimus-eluting stent