The Zotarolimus-eluting Endeavor sprint stent in Uncertain DES candidates (ZEUS)

M. Valgimigli, MD, PhD

Erasmus MC, Rotterdam

The Netherlands

On behalf of the ZEUS Investigators

I, Marco Valgimigli, have received:

- honoraria for lectures/advisory board from Merck, Correvio, Eli Lilly, Astra Zeneca, The Medicines Company, St Jude, Abbott Vascular, CID and Terumo.
- Institutional research grant from Medtronic (current study), The Medicines Company, Terumo

ZEUS

Background

- Drug-eluting stents (DES) *per se* are currently regarded as more efficacious but also more thrombogenic than BMS
- In order to restore safety to a level comparable to BMS, a prolonged course of dual antiplatelet therapy (DAPT) has been recommended after DES

ZEUS

Background

- **As a consequence, the use of DES instead of BMS remains controversial in selected patient/lesion subsets:**

- **Pts at high bleeding risk**
  - ***in whom long-term DAPT poses safety concerns***
- **Pts at high thrombosis risk**
  - ***whose risk for coronary events may be higher after DES***
- **Pts at low risk for in-stent restenosis**
  - ***the need for prolonged DAPT and the long-term risk for adverse events after DES implantation may outweigh their benefit in terms of low re-intervention rates***

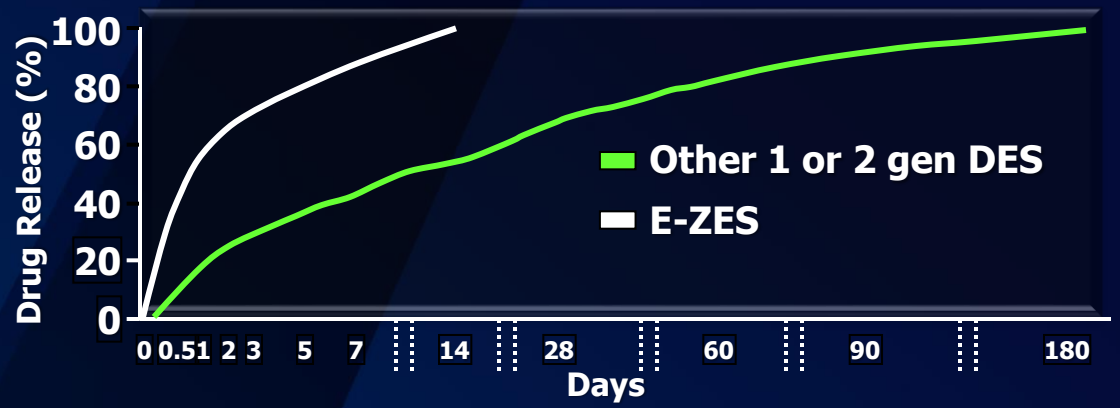
Systematically Excluded from RCTs

ZEUS

Zotarolimus-eluting Endeavor Sprint:

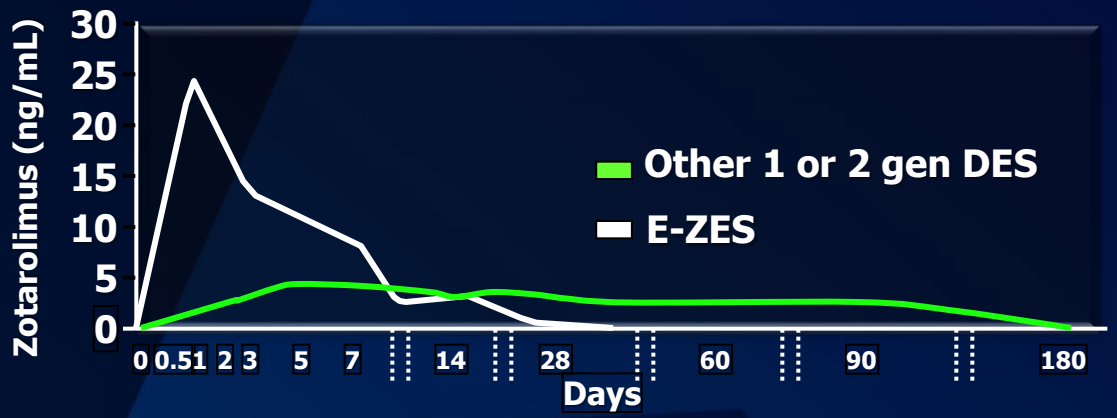
hydrophilic polymer-based second-generation device with unique drug fast-release profile

Drug Elution Kinetics



ZES (PC-Coating)
100% Eluted at 14 days

Zotarolimus in Arterial Tissue (in Stent)



No detectable drug in arterial tissue beyond 28 days

EuroInterv.2007;3:50-53

ZEUS

Study Design

Am Heart J. 2013 Nov;166(5):831-8

Urgent or emergent coronary stenting in pts fulfilling ≥1 of the below:

High Bleeding Risk
- Need for OACs
- Previous Relevant Bleeding
- Age > 80 y/o
- Bleeding diathesis
- Known Anemia (Hb<10 gr/dl)
- Need for CCS or NSAID

High Thrombotic Risk
- Intolerance to ASA
- Intolerance to any $P2Y_{12}$
- Planned surgery w/in 1 year
- Cancer-life expectancy >1 Y
- Pro-thrombotic diathesis

Low Restenosis Risk
- Planned stent ≥3.0 mm, apart from LMCA and SVG intervention or for ISR lesions

Rx: 1:1, *Sx: inclusion criteria*

1,606 pts, 20 sites in *Italy*, *Switzerland*, *Portugal* and Hungary from June 2011 to September 2012

Endeavor Sprint Zotarolimus-eluting Stent

Thin-strut Bare Metal Stent

Primary Endpoint: Death, Myocardial Infarction or Target Vessel Revascularization at 12 months

ZEUS

Study Design

Am Heart J. 2013 Nov;166(5):831-8

Urgent or emergent coronary stenting in pts fulfilling ≥1 of the below:

High Bleeding Risk
- Need for OACs
- Previous Relevant Bleeding
- Age > 80 y/o
- Bleeding diathesis
- Known Anemia (Hb<10 gr/dl)
- Need for CCS or NSAID

High Thrombotic Risk
- Intolerance to ASA
- Intolerance to any $P2Y_{12}$
- Planned surgery w/in 1 year
- Cancer-life expectancy >1 Y
- Pro-thrombotic diathesis

Low Restenosis Risk
- Planned stent ≥3.0 mm, apart from LMCA and SVG intervention or for ISR lesions

Rx: 1:1, ***Sx: inclusion criteria***

1,606 pts, 20 sites in *Italy*, *Switzerland*, *Portugal* and Hungary from June 2011 to September 2012

Endeavor Sprint Zotarolimus-eluting Stent

Thin-strut Bare Metal Stent

***Personalised DAPT duration*, i.e. modelled according to the patient clinical risk profile and not by stent type**

ZEUS

Study Design

Am Heart J. 2013 Nov;166(5):831-8

Urgent or emergent coronary stenting in pts fulfilling ≥1 of the below:

High Bleeding Risk
- Need for OACs
- Previous Relevant Bleeding
- Age > 80 y/o
- Bleeding diathesis
- Known Anemia (Hb<10 gr/dl)
- Need for CCS or NSAID

DAPT:
30 days

High Thrombotic Risk
- Intolerance to ASA
- Intolerance to any $P2Y_{12}$
- Planned surgery w/in 1 year
- Cancer-life expectancy >1 Y
- Pro-thrombotic diathesis

DAPT:
None if **ASA/$P2Y_{12}$i intol.**
Up to surgery **if planned**
≥ 6 mos **in others**

Low Restenosis Risk
- Planned stent ≥3.0 mm, apart from LMCA and SVG intervention or for ISR lesions

DAPT:
Stable CAD *30 days*
ACS ≥ *6 mos*

ZEUS

Napoli—C. Briguori

Szeged— A. Thury, I. Ungi

Torino—S. Colangelo; R. Garbo

Parma—A. Menozzi

Zingonia—N. de Cesare

Torino—E. Meliga

Baggiovara —S. Tondi

Geneva—M. Roffi

Arezzo—F. Liistro

Milano— L. Testa, F. Bedogni

Pavia—M. Ferlini

Lisbon— H. M. Gabriel

Milano—F. Airoldi

Savigliano—A. Dellavalle

Bergamo—G. Musumeci

Ravenna—M. Acquilina

Ferrara—Sponsor and study site
with an unrestricted grant from Medtronic

Clinical Event Committee

P. Vranckx, *Chair*

S. Curello

G. Guardigli

Angiographic Core-lab

A. Patialiakas, Chair

Data Management and Monitoring

Medical Trial Analysis

Eustrategy Research Coordination

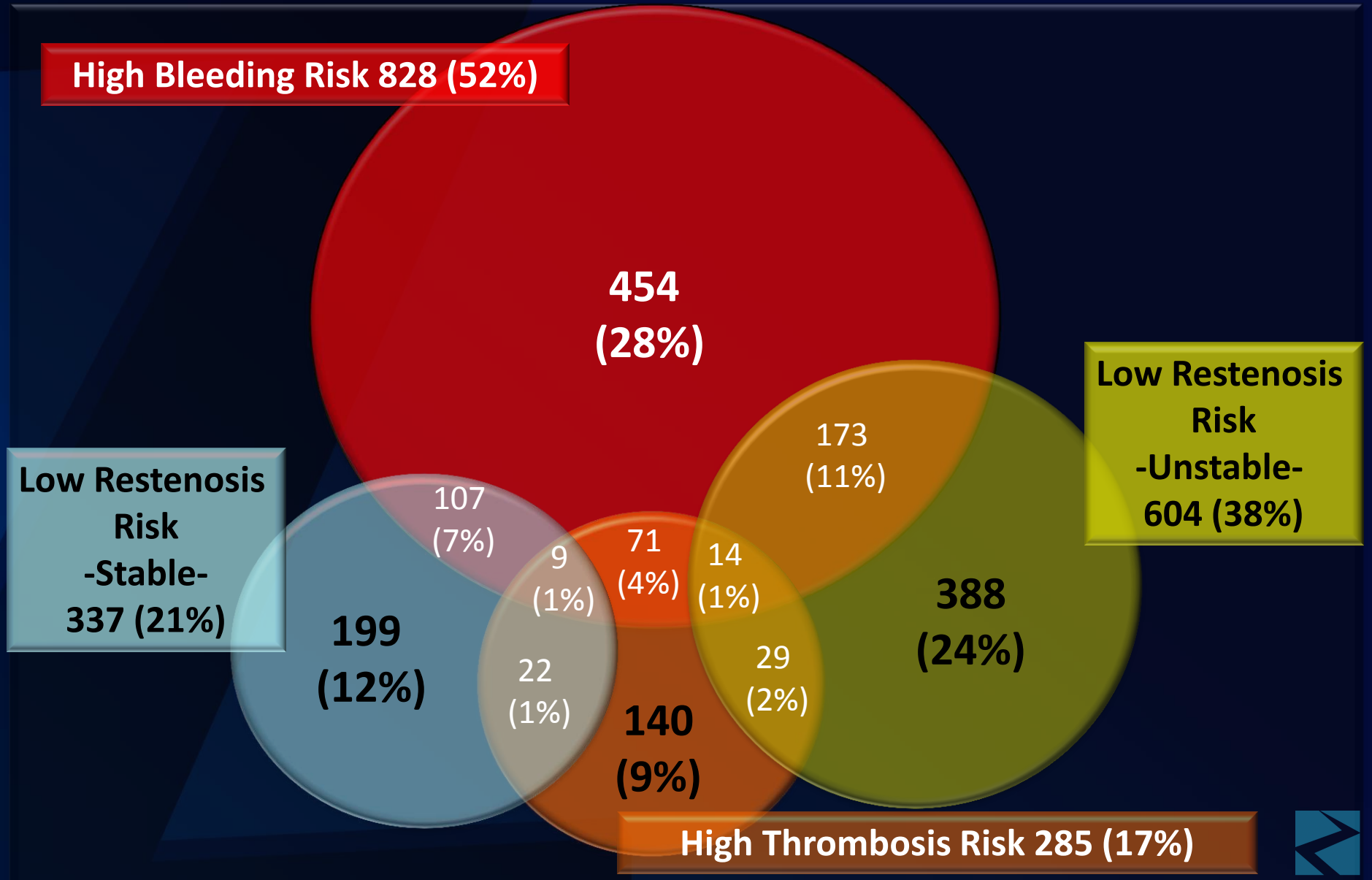
Key baseline or angiographic features of the study population *(N=1,606)*

	BMS (N=804)	E-ZES (N=802)
Age, median (IQR)	74 (64-81)	74 (64-81)
Females (%)	29	30
Diabetes (%)	26	27
Prior MI/PCI/CABG (%)	24/19/7	24/19/7
Mild to Severe CKD (%)	41	42
ACS/STEMI (%)	63/19	63/ 19
MVD (%)	61	59
LAD/LMCA treated (%)	51/5	53/5
≥1 B2/C treated lesion (%)	73	73

MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; CKD: chronic kidney dysfunction; Lad: left anterior descending, LMCA: left main coronary artery; ACS: acute coronary syndrome; STEMI: ST-segment elevation myocardial infarction

ZEUS

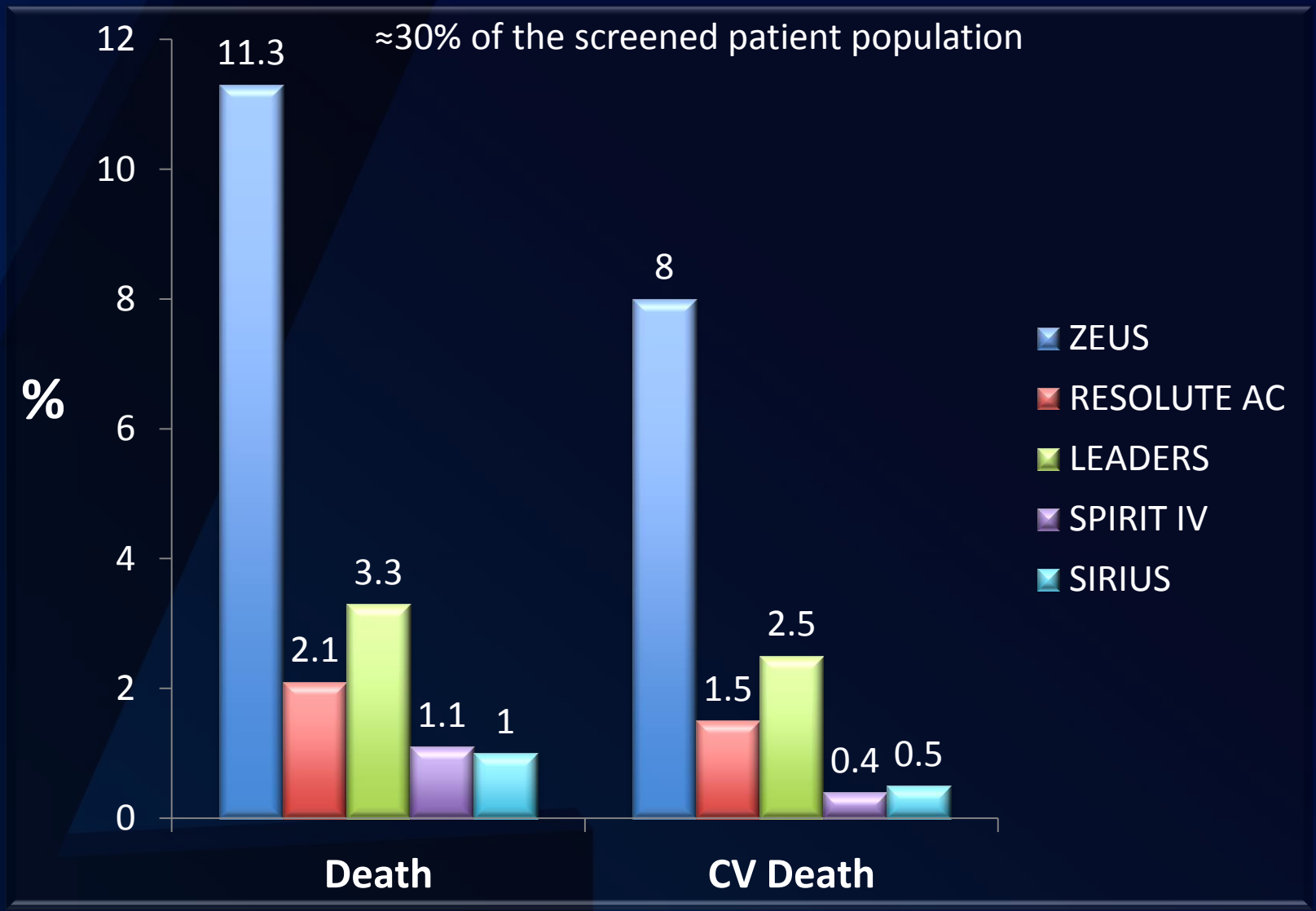
Study Population



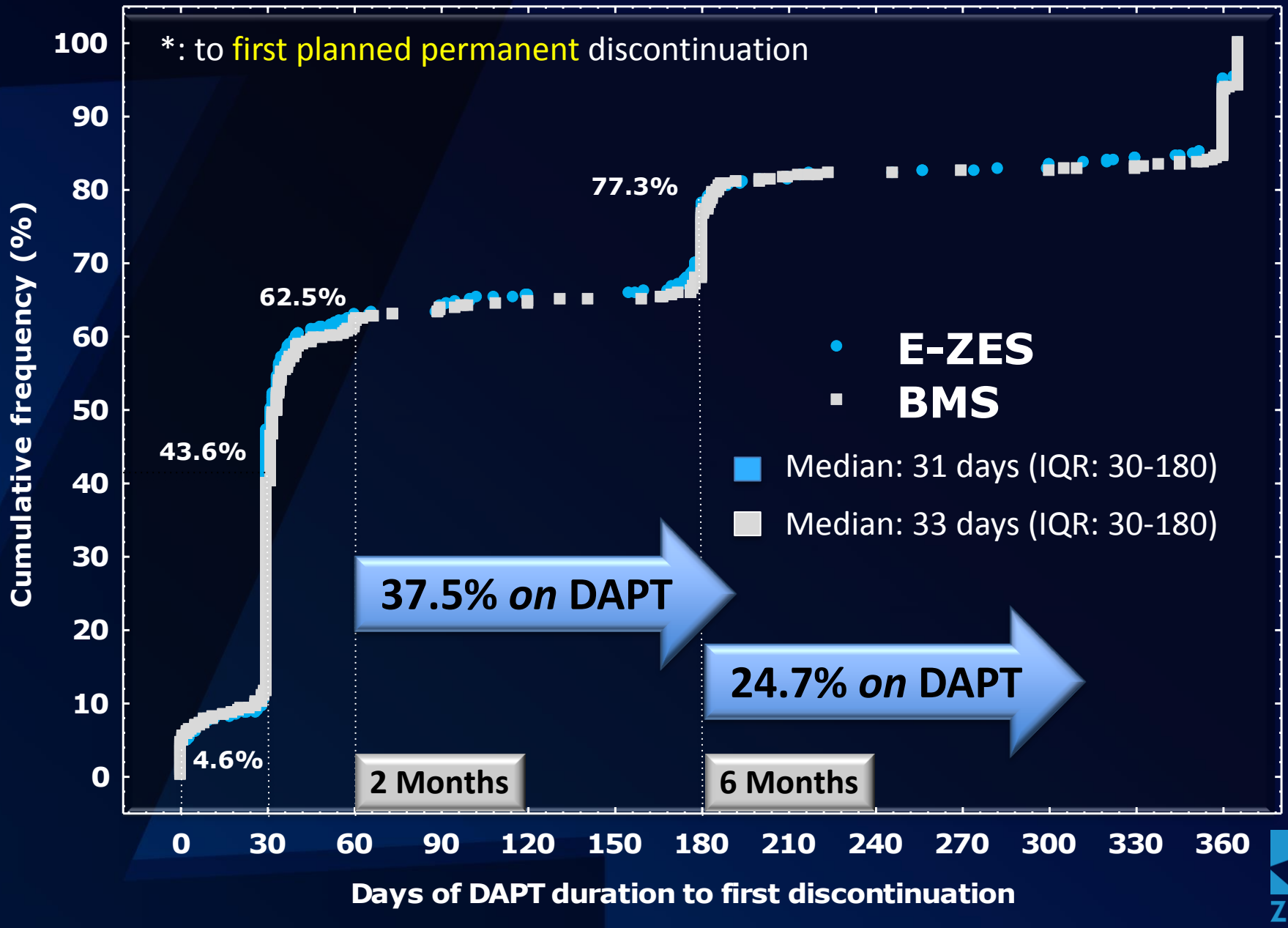
ZEUS

ZEUS: Truly high risk patient population

Event rates at 1 year across stent trials



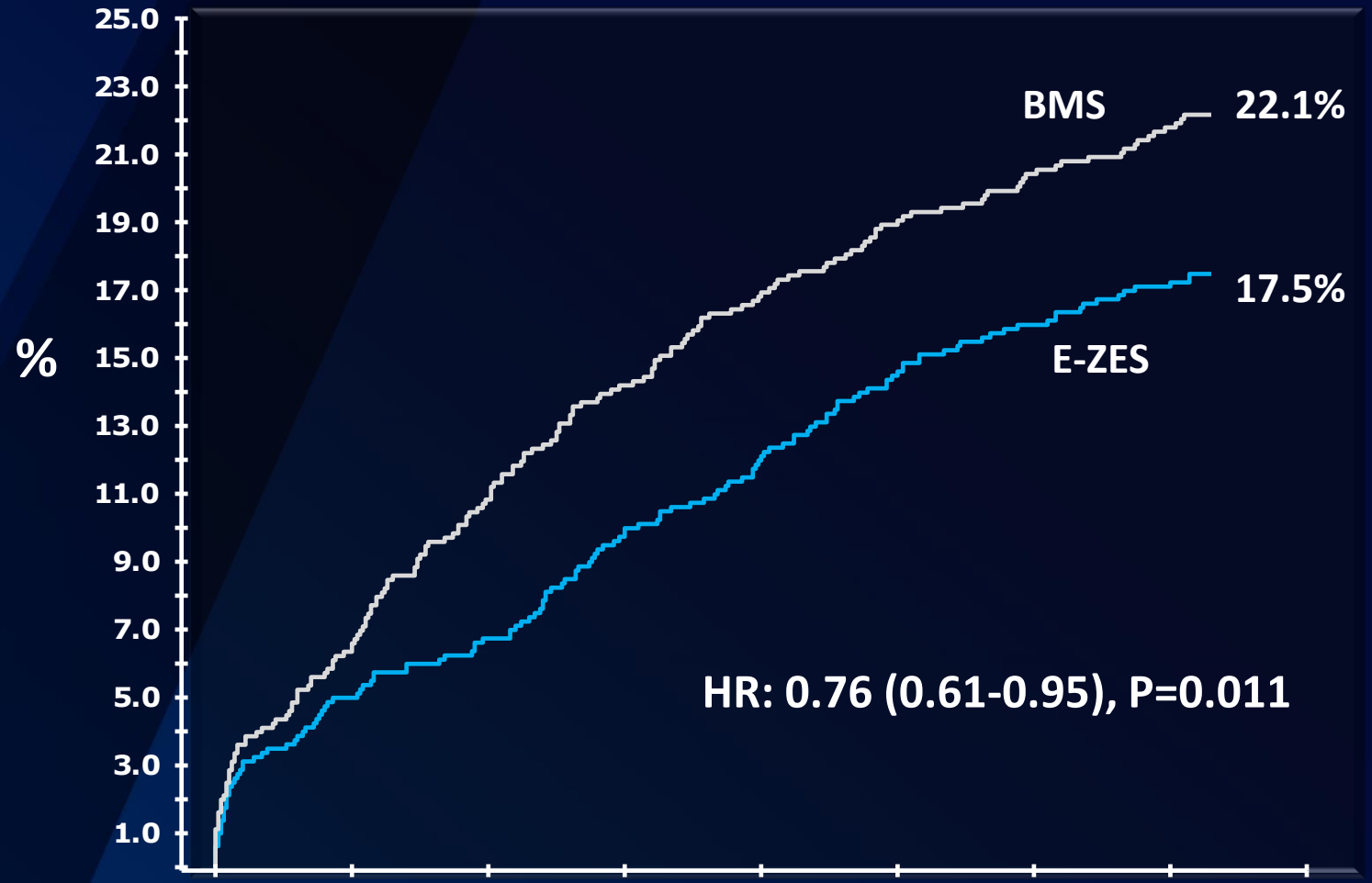
Duration of DAPT* in stent groups (ITT)



ZEUS

Major Adverse Cardiovascular events

primary endpoint

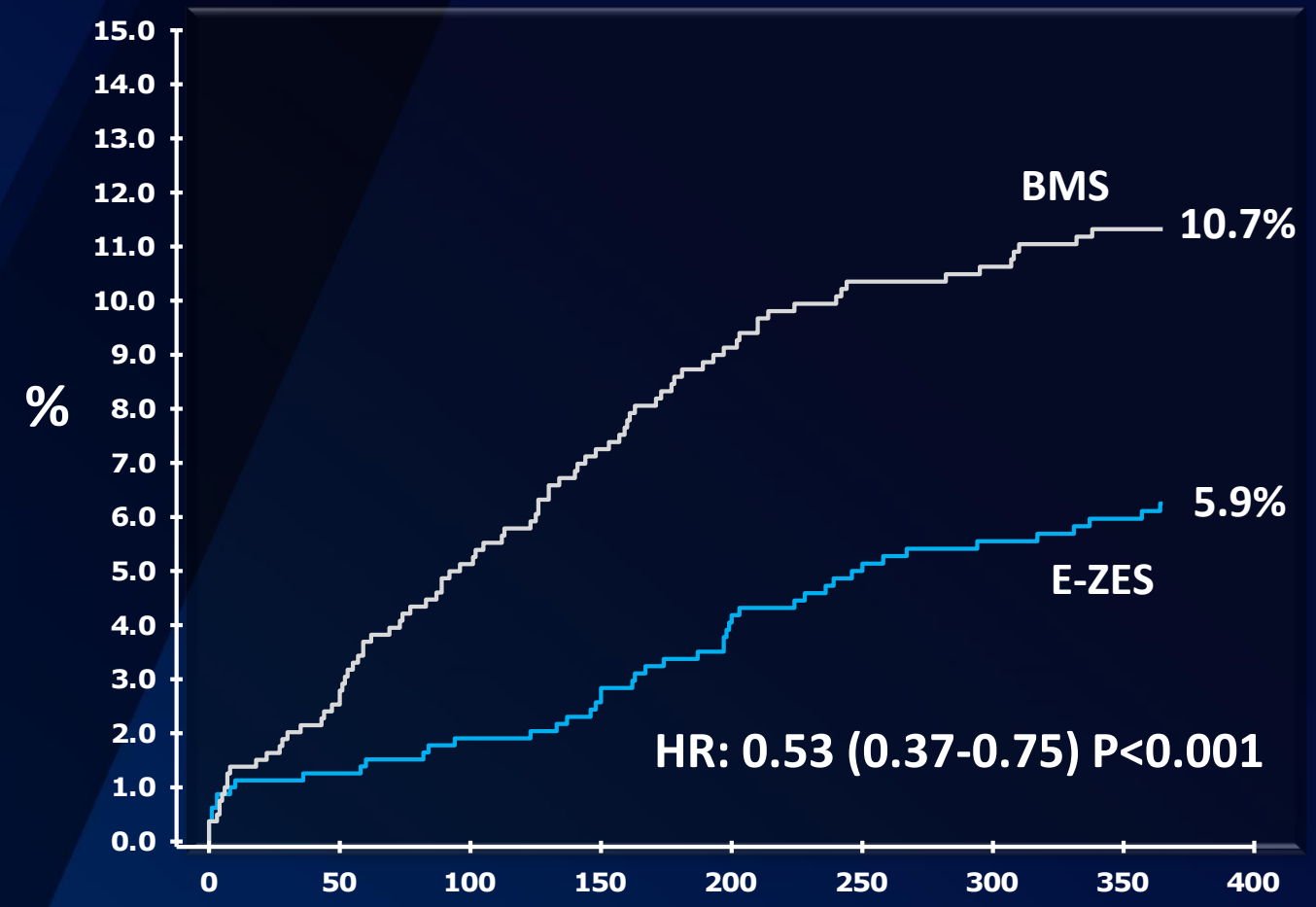


No. at Risk								
BMS	804	752	716	689	668	651	639	628
E-ZES	802	761	747	723	705	685	673	664

2 pts, one in each group, were lost to follow-up after hospital discharge

ZEUS

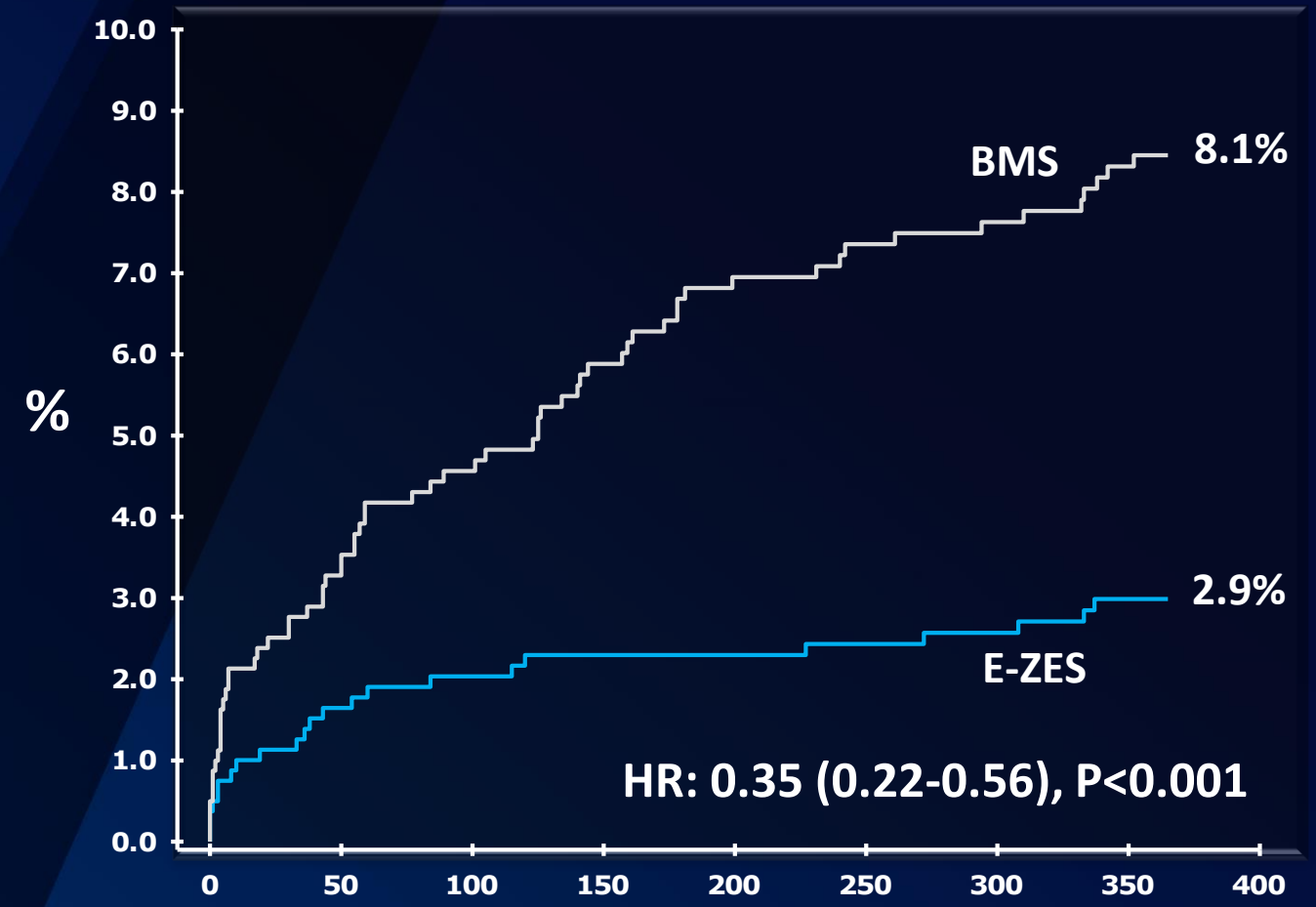
Target Vessel Revascularization



No. at Risk								
BMS	804	759	721	694	675	657	645	636
E-ZES	802	765	751	729	712	693	682	675

ZEUS

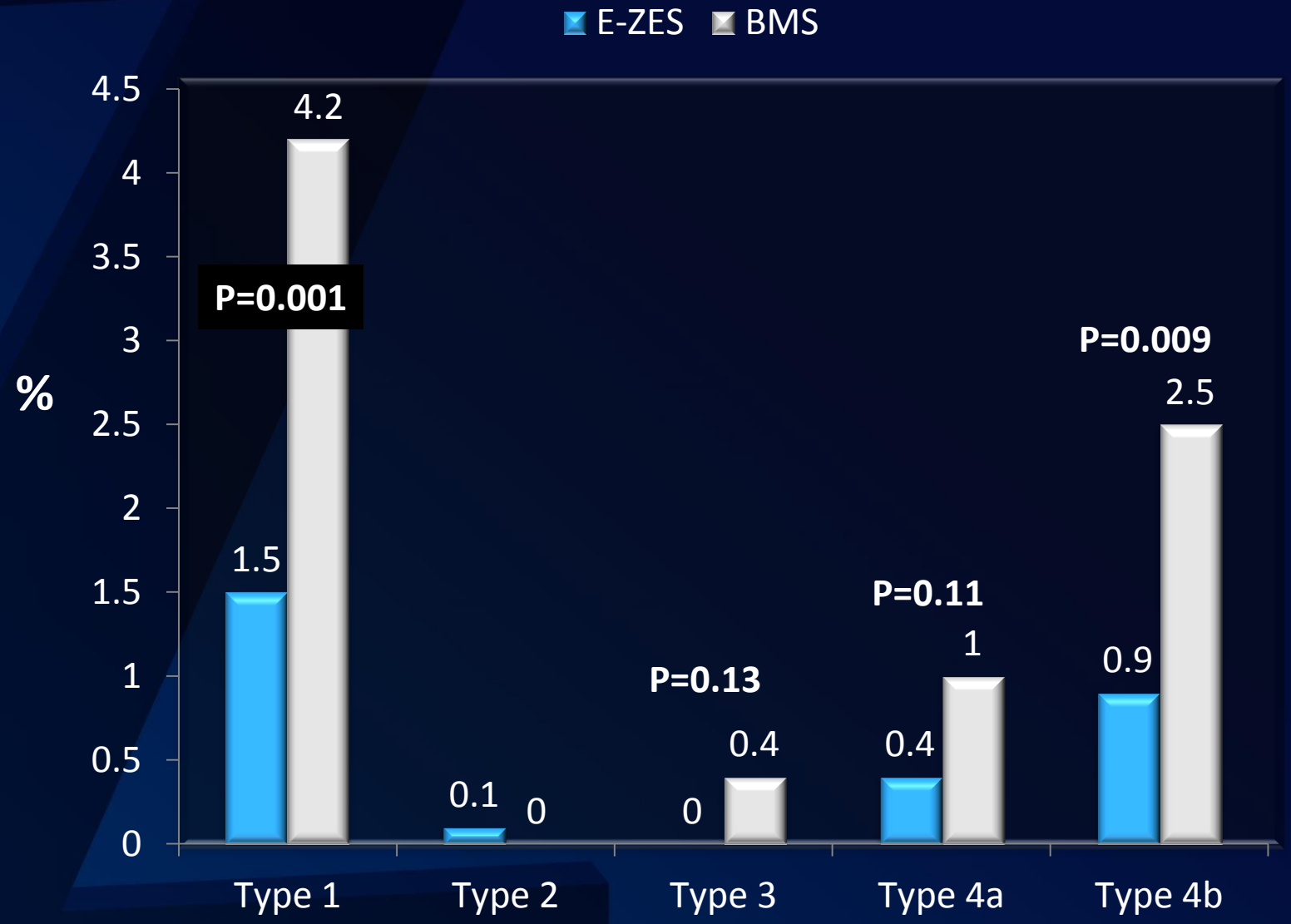
Myocardial infarction



No. at Risk								
BMS	804	757	730	709	695	684	675	666
E-ZES	802	762	750	733	726	713	698	684

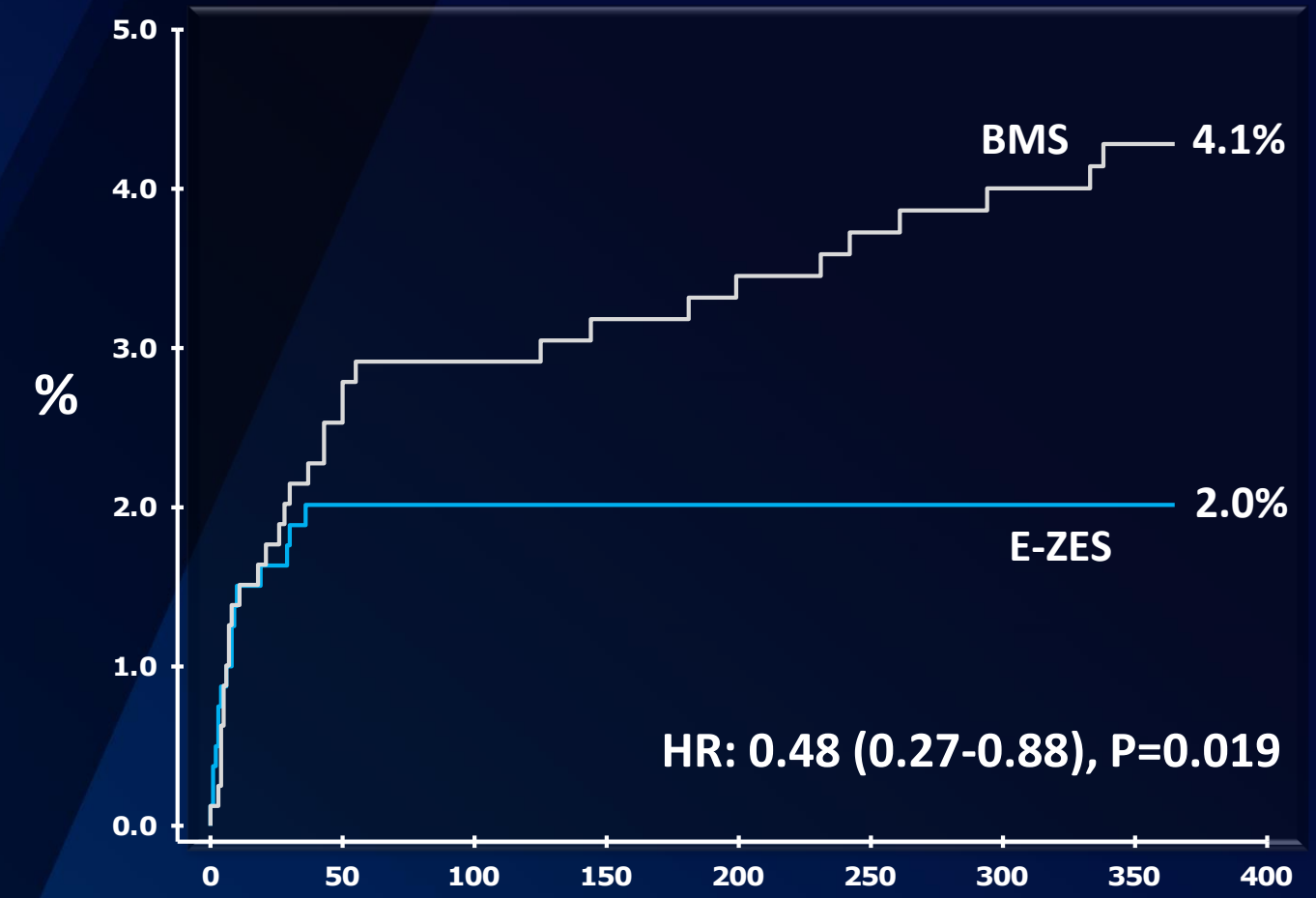
ZEUS

An application of the Classification System from the Universal MI Definition



ZEUS

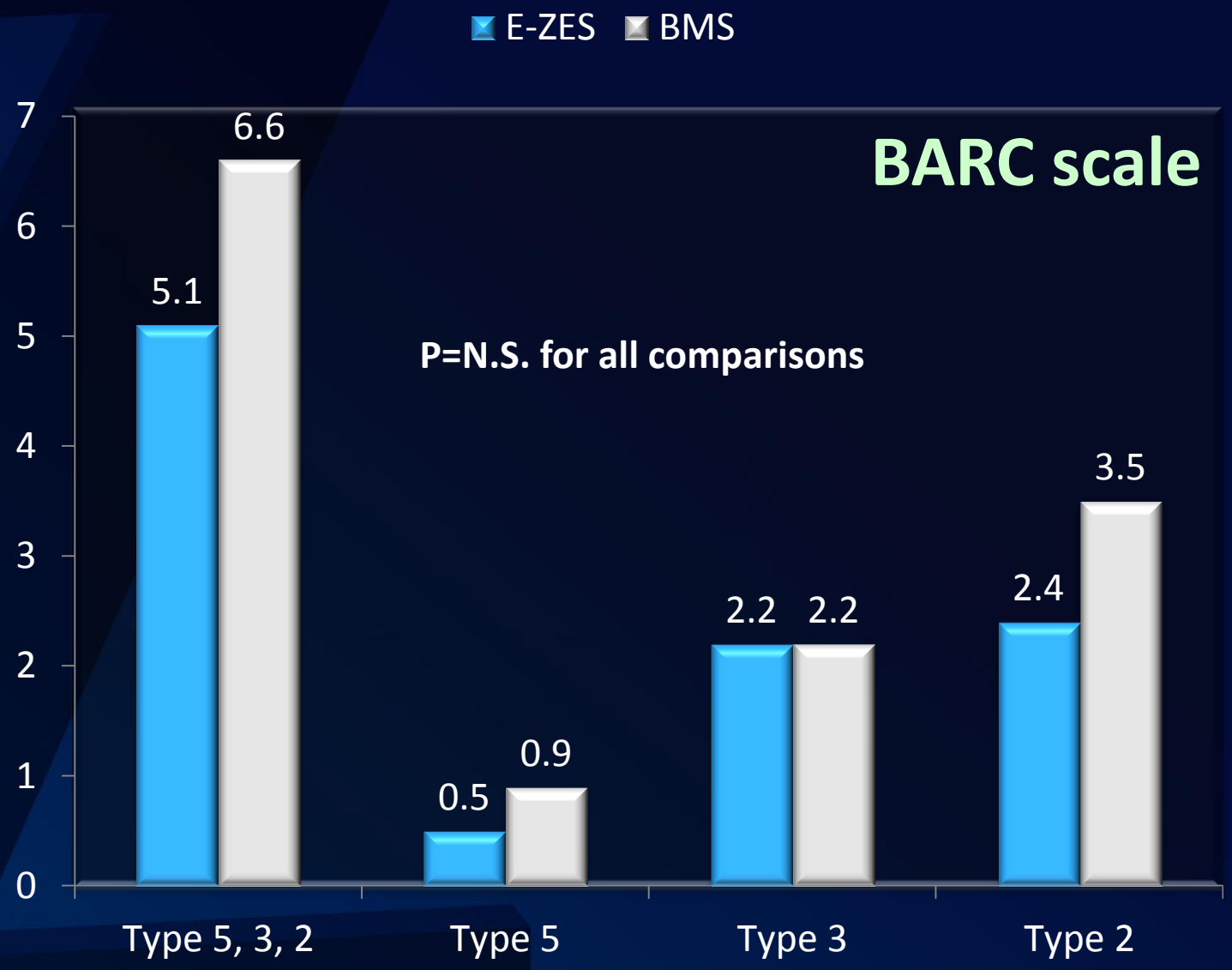
Definite or Probable Stent Thrombosis



No. at Risk								
BMS	804	763	739	723	712	701	692	685
E-ZES	802	767	758	741	733	721	713	708

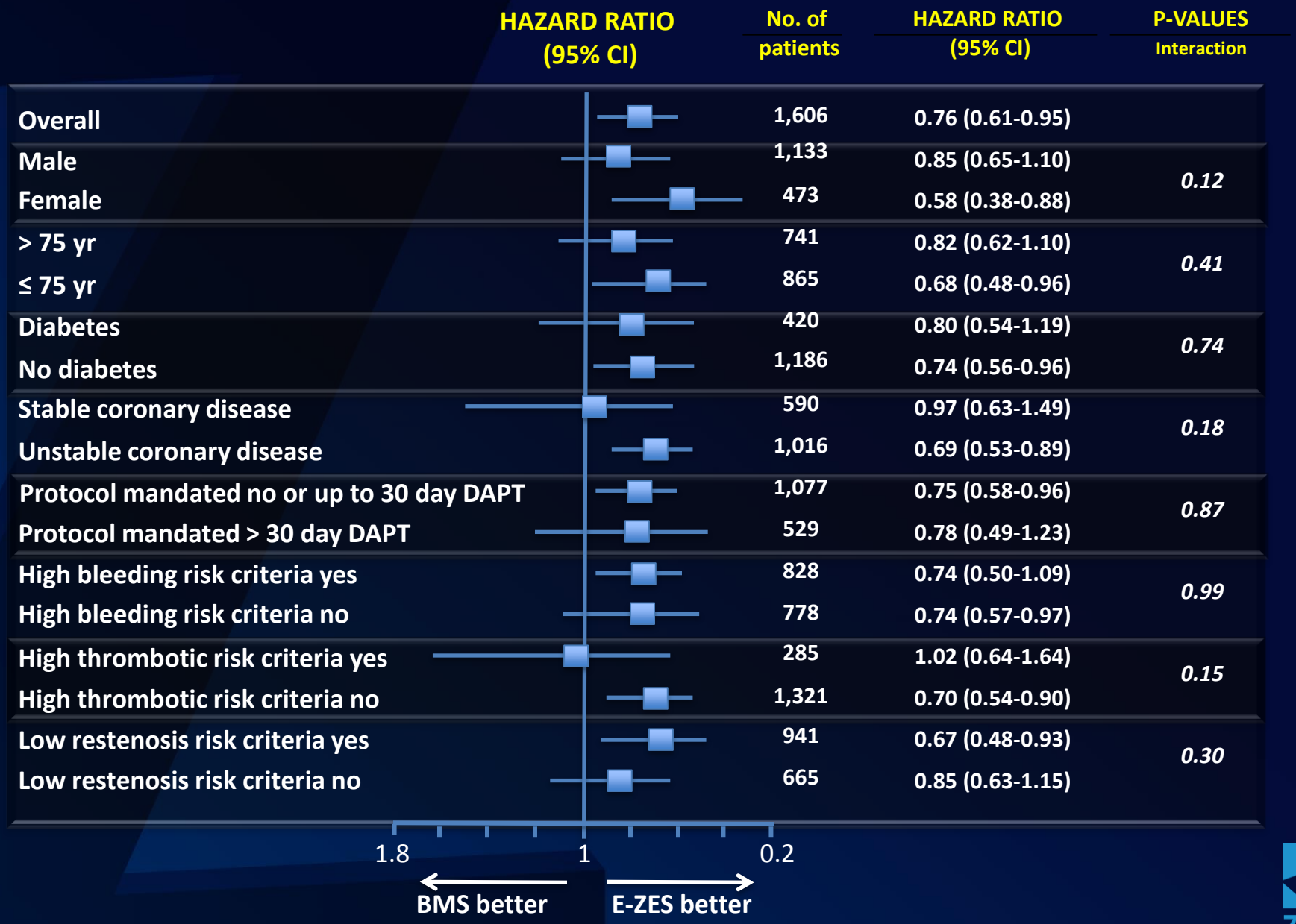
ZEUS

Bleeding events in the two groups



ZEUS

Subgroup Analysis for the Primary Endpoint



ZEUS

Conclusions

- In patients at high bleeding, thrombotic or low restenosis risk, E-ZES implantation followed by a personalized duration of DAPT, including no or a 30-day course of therapy, resulted in a lower risk of major adverse cardiovascular events as compared to BMS
- Our study suggests that E-ZES may become the new gold standard coronary device in pts who cannot, or refuse to, tolerate (long-term) DAPT

ZEUS