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Two-Year Outcomes of High Bleeding Risk Patients after Polymer-Free Drug-Coated Stents

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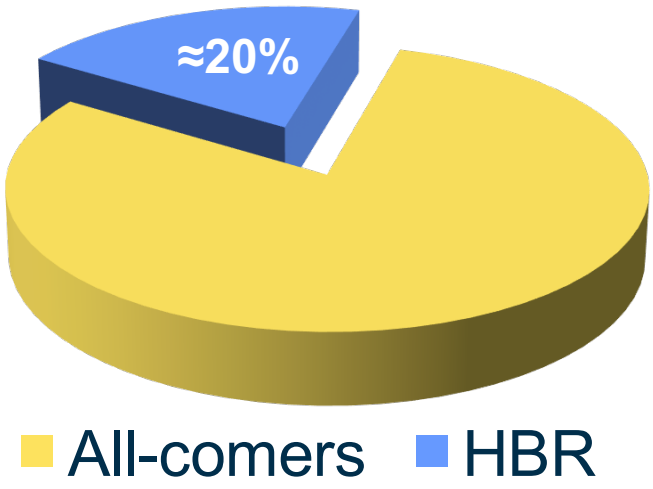
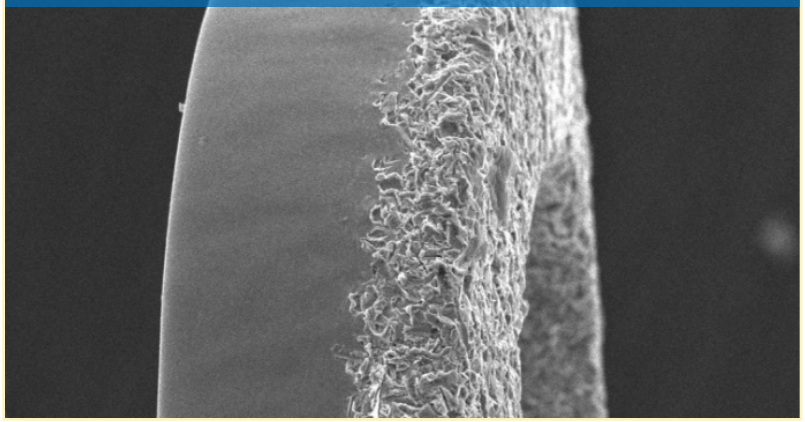
High Bleeding Risk Patients (HBR)

- Mostly excluded from device and APT trials
- Never specifically studied
- Current guideline recommendations:
  - BMS + one month DAPT
  - DES + “shortened” DAPT

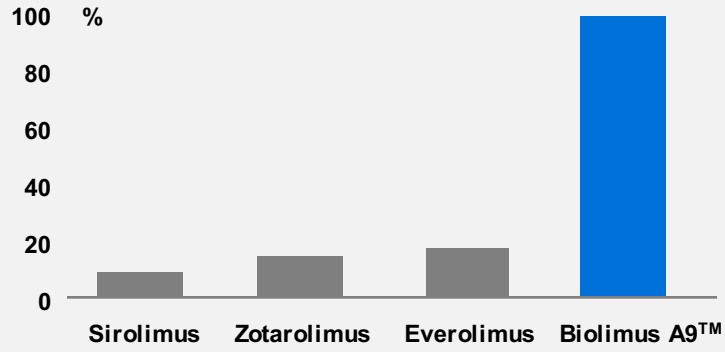


BioFreedom™ Drug Coated Stent (DCS)

Selectively Micro-Structured Surface Holds Drug in Abluminal Surface Structures



BA9™ Drug 10 Times More Lipophilic than Sirolimus[1]



+/- 2.8% (valid for all drugs test)

Advantages:

- Avoid any possible polymer-related adverse effects
- Rapid drug transfer to vessel wall (98% within one month[2])
- Good fit with short DAPT

1. Data on file at Biosensors Intl;
2. Tada et al., Circ Cardiovasc Interv 2010;3;174-183

LEADERS FREE Trial Design

Prospective, double-blind randomized (1:1) trial
2466 High bleeding risk (HBR) PCI patients

BioFreedom™ DCS	VS.	Gazelle™ BMS

DAPT mandated for 1 month only, followed by long-term SAPT

- **Primary safety endpoint:**
  Composite of cardiac death, MI, definite / probable stent thrombosis at 1 year (non-inferiority then superiority)
- **Primary efficacy endpoint:**
  Clinically-driven TLR at 1 year (superiority)

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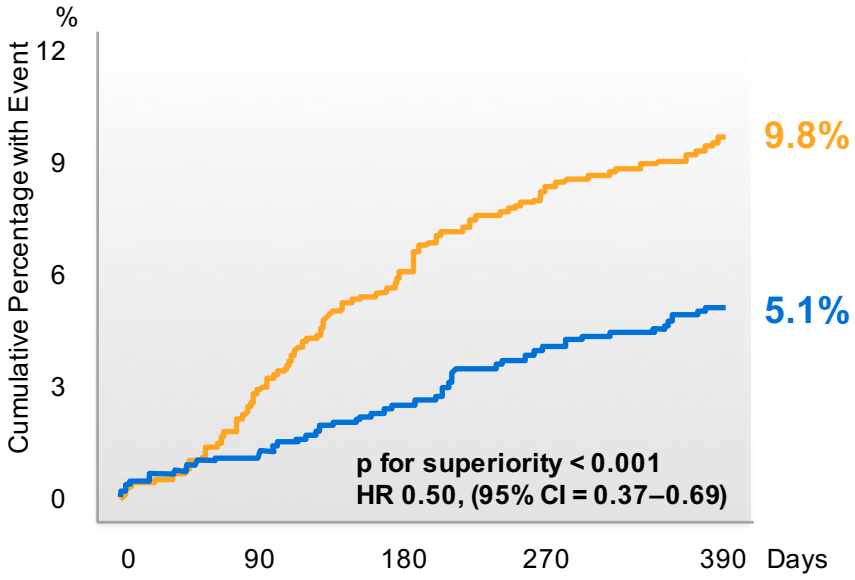
Primary Endpoints at 1 Year

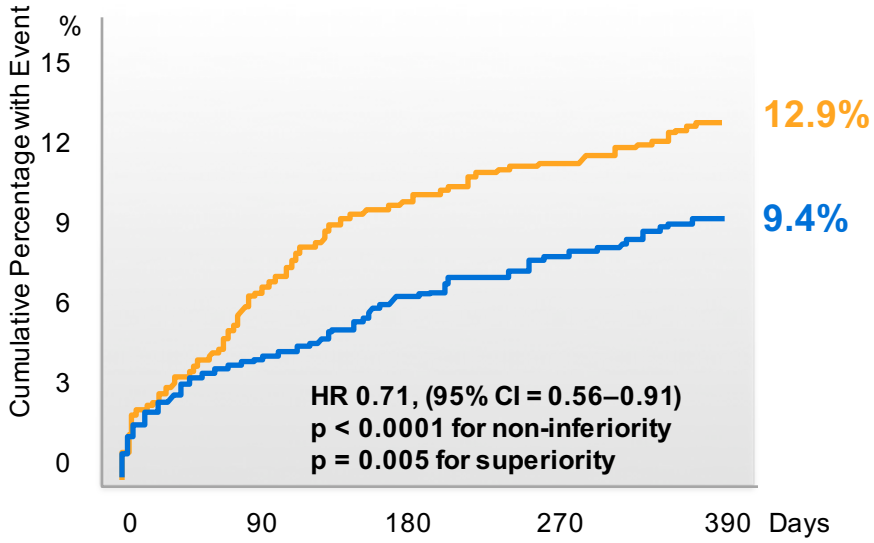
Efficacy (cd-TLR)

DCS BMS



Safety (cardiac death, MI, ST)

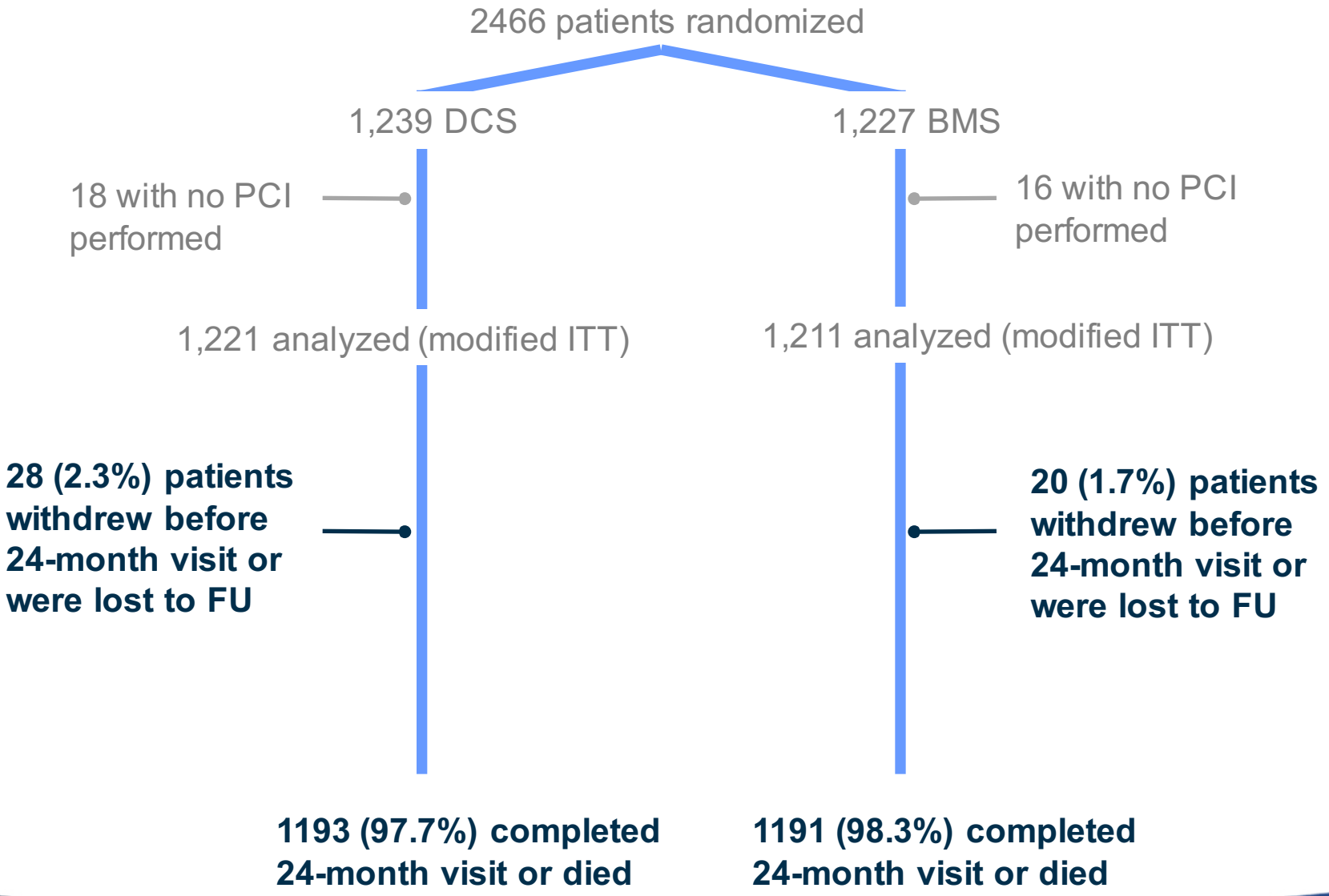
DCS BMS



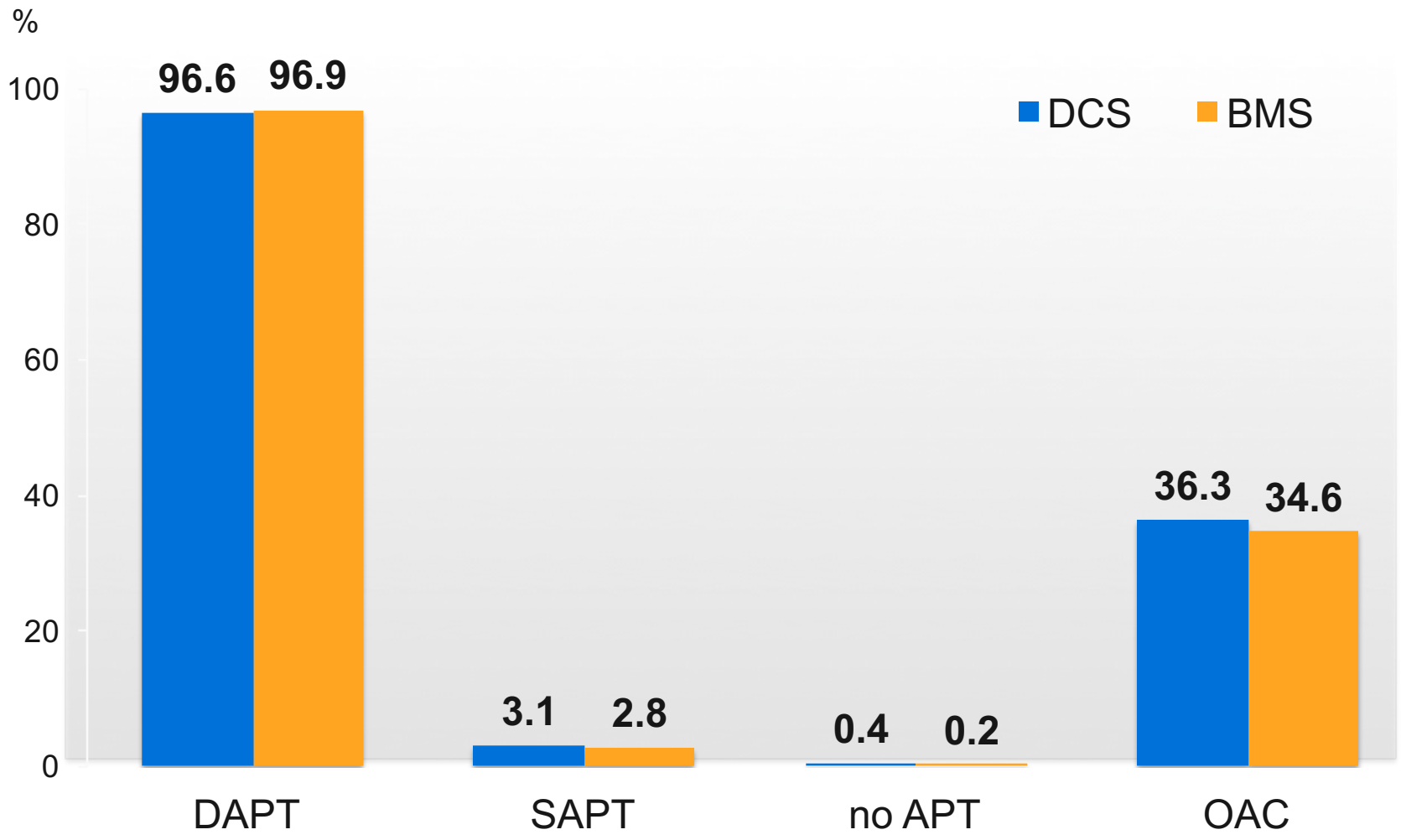
Urban P et al. N Engl J Med 2015;373:2038-47

Two Year Follow-up

Enrollment and Follow-Up



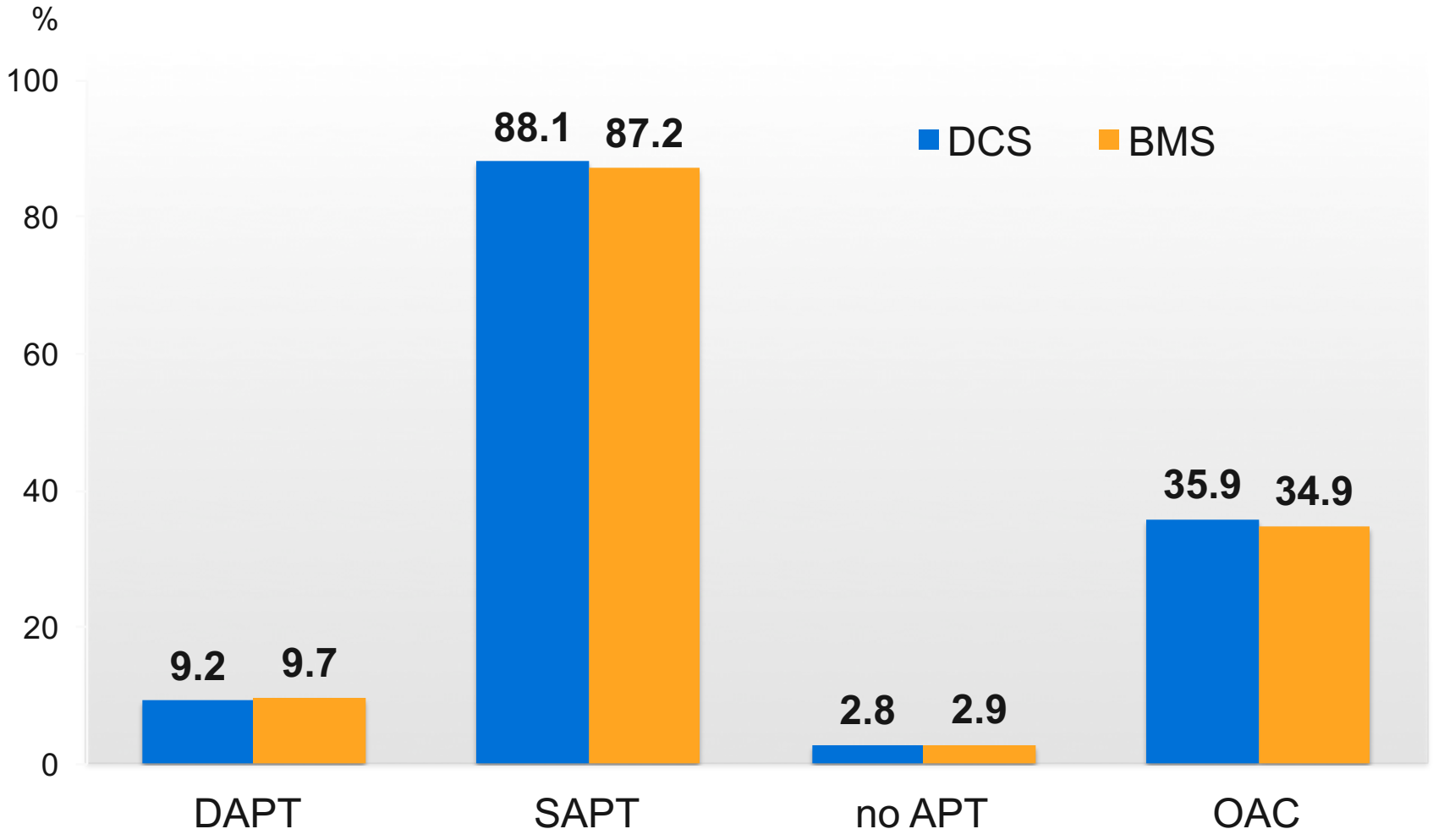
Antithrombotic Medication at Discharge



None of the regimens differ at $p < 0.05$

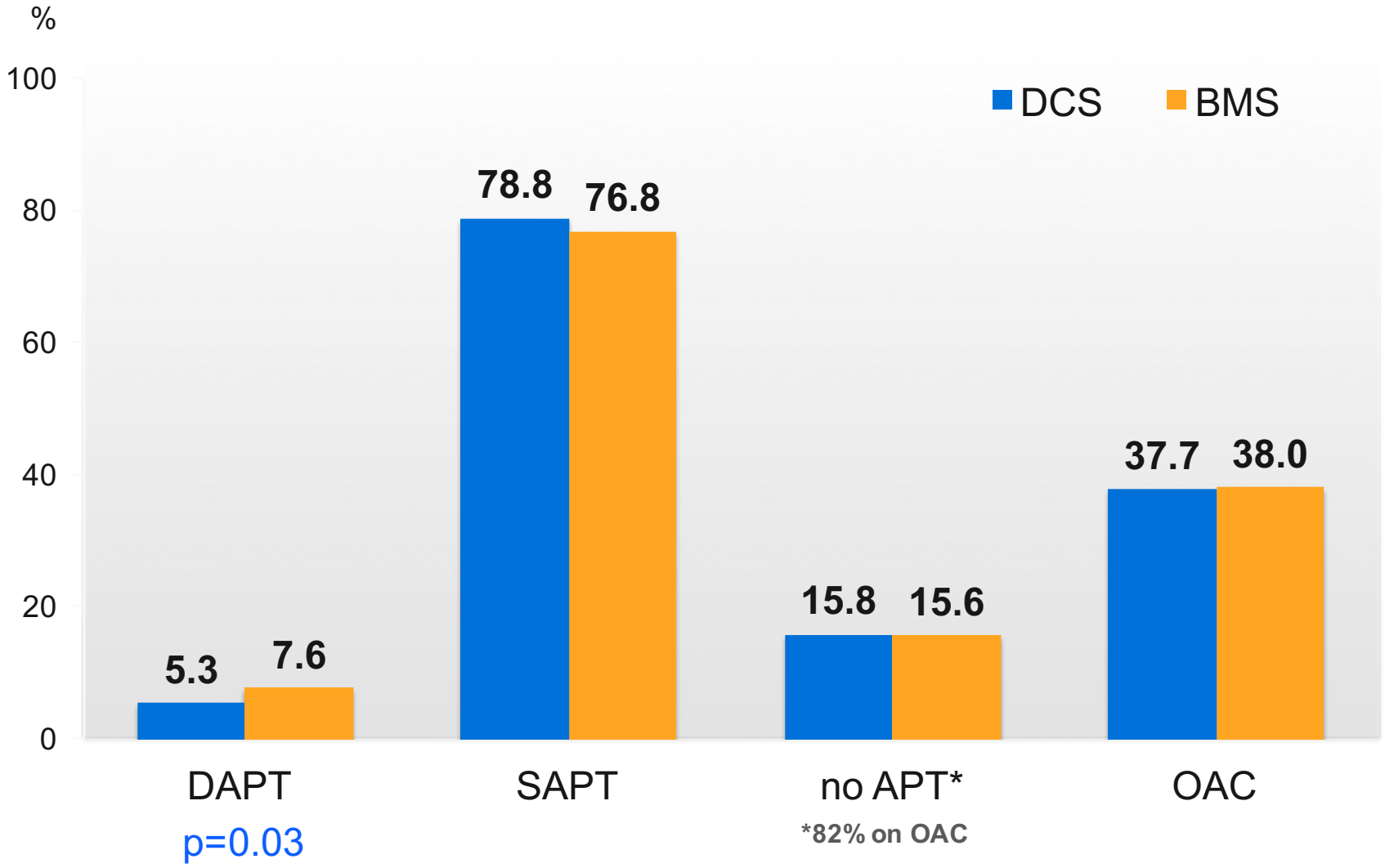
Antithrombotic Medication after 1 month visit*

* at day 37

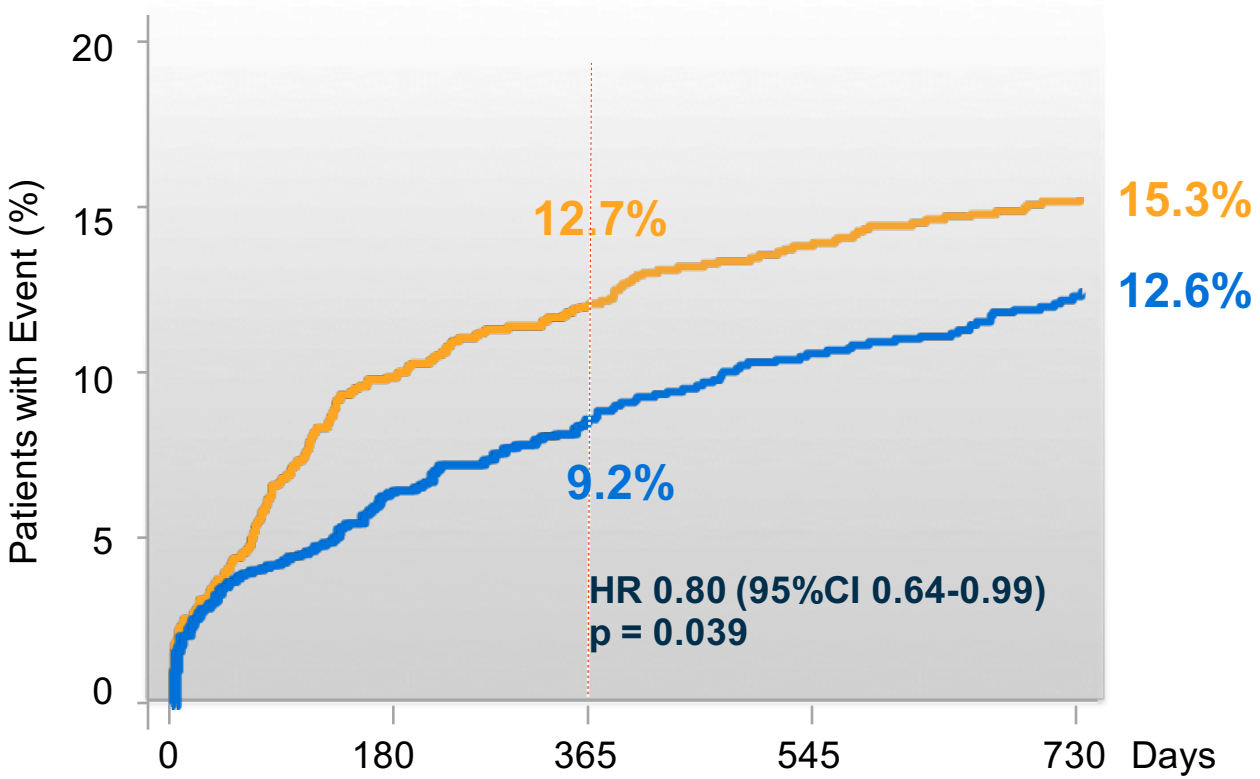


None of the regimens differ at $p < 0.05$

Antithrombotic Medication at 2 years



Primary Safety Endpoint
(Cardiac Death, MI, ST) at 2 year

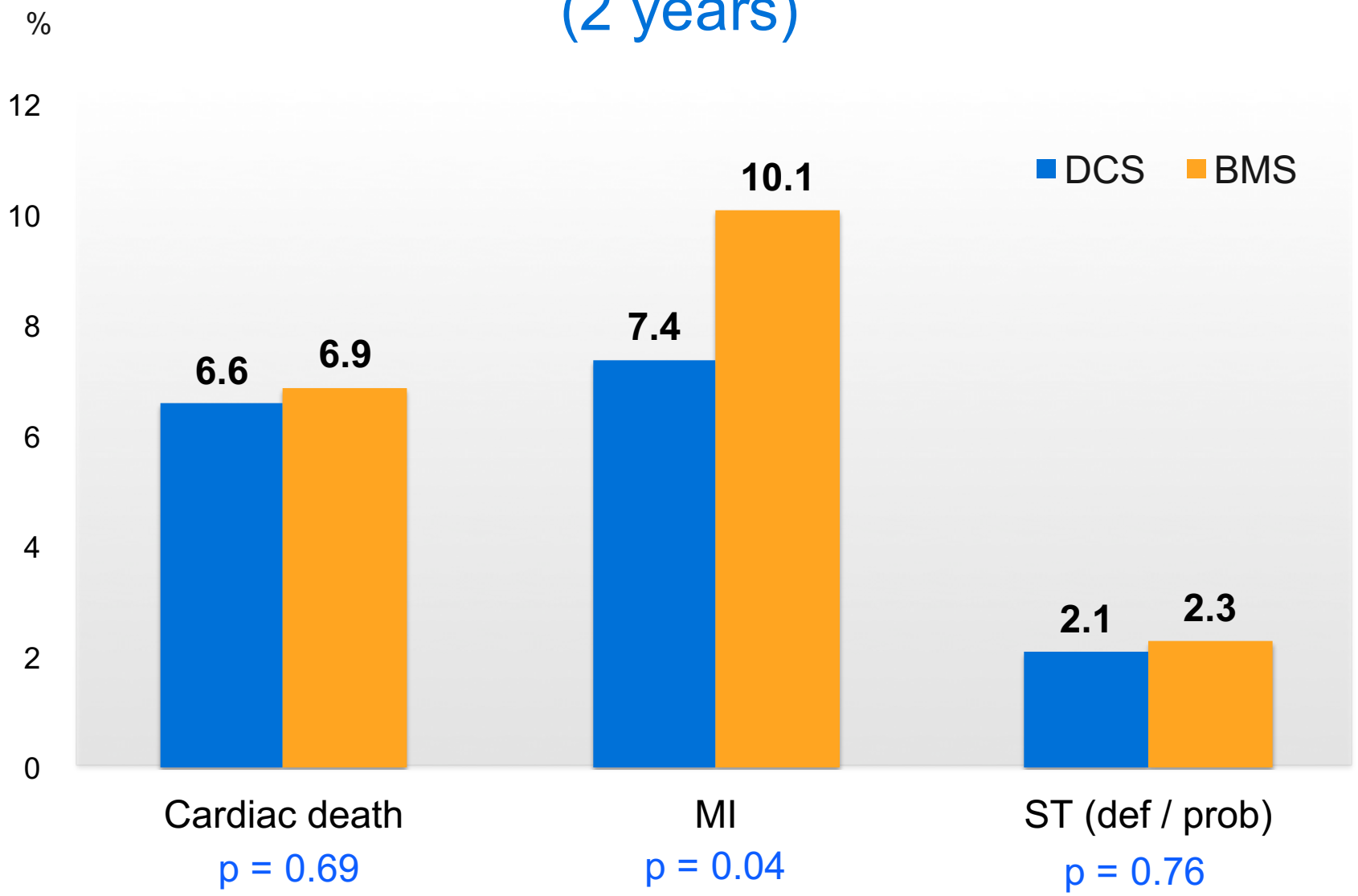


Number at Risk

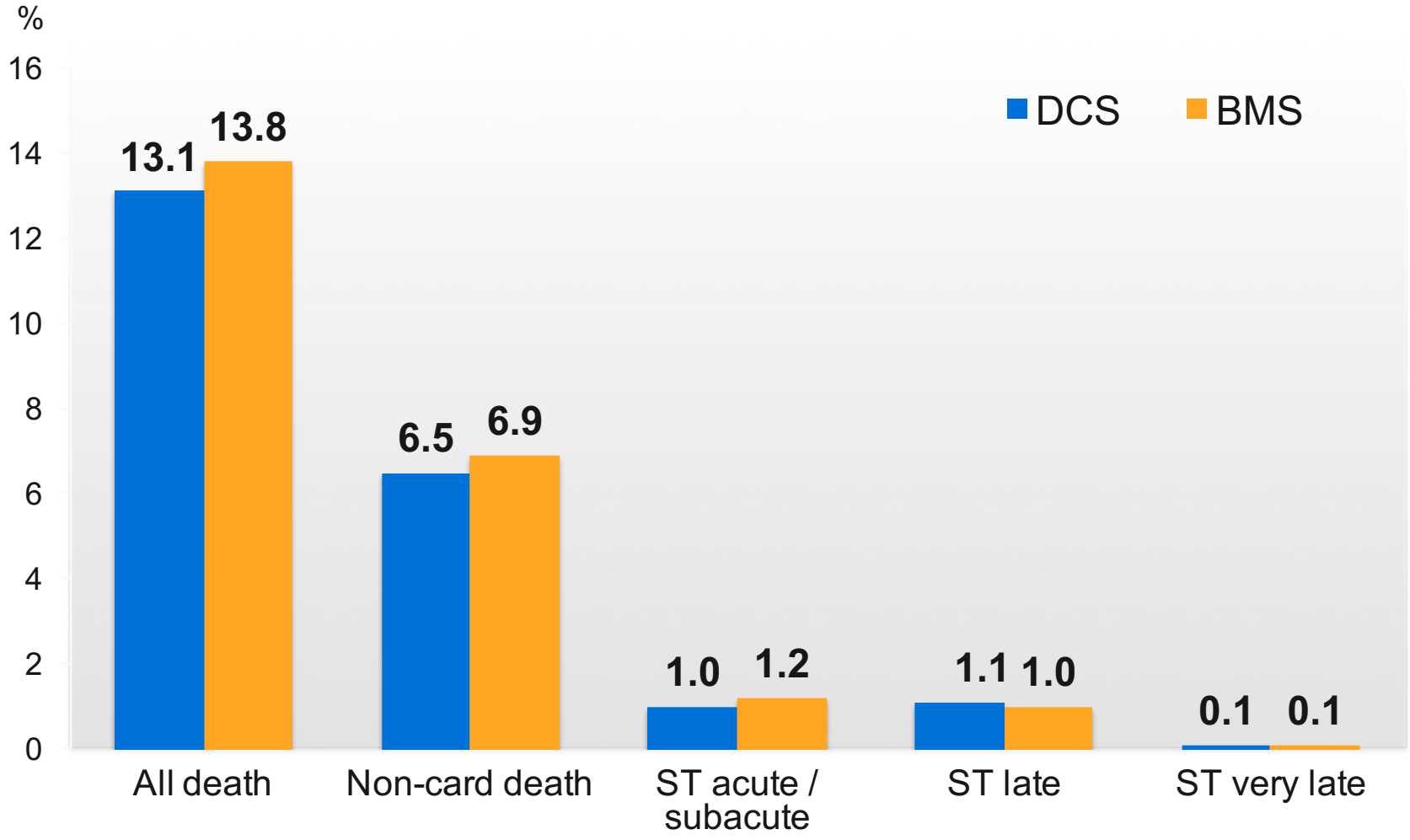
DCS	1221	1104	1052	1006	620
BMS	1211	1067	1010	973	587

2 year FU was obtained at 730 days ± 60 days

Components of Safety Endpoint
(2 years)

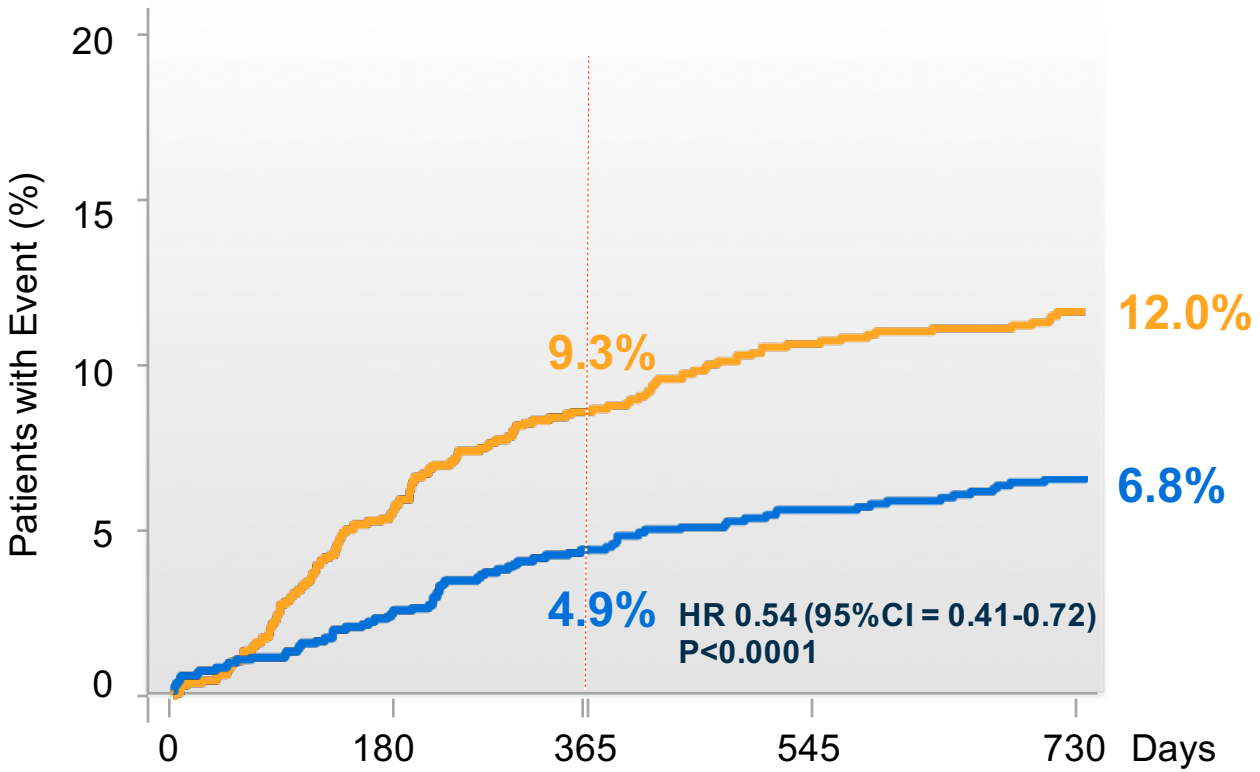


Selected Secondary Safety Endpoints
(2 years)



None of these endpoints differ at $p < 0.05$

Primary Efficacy Endpoint
(Clinically-Driven TLR) at 2 Years

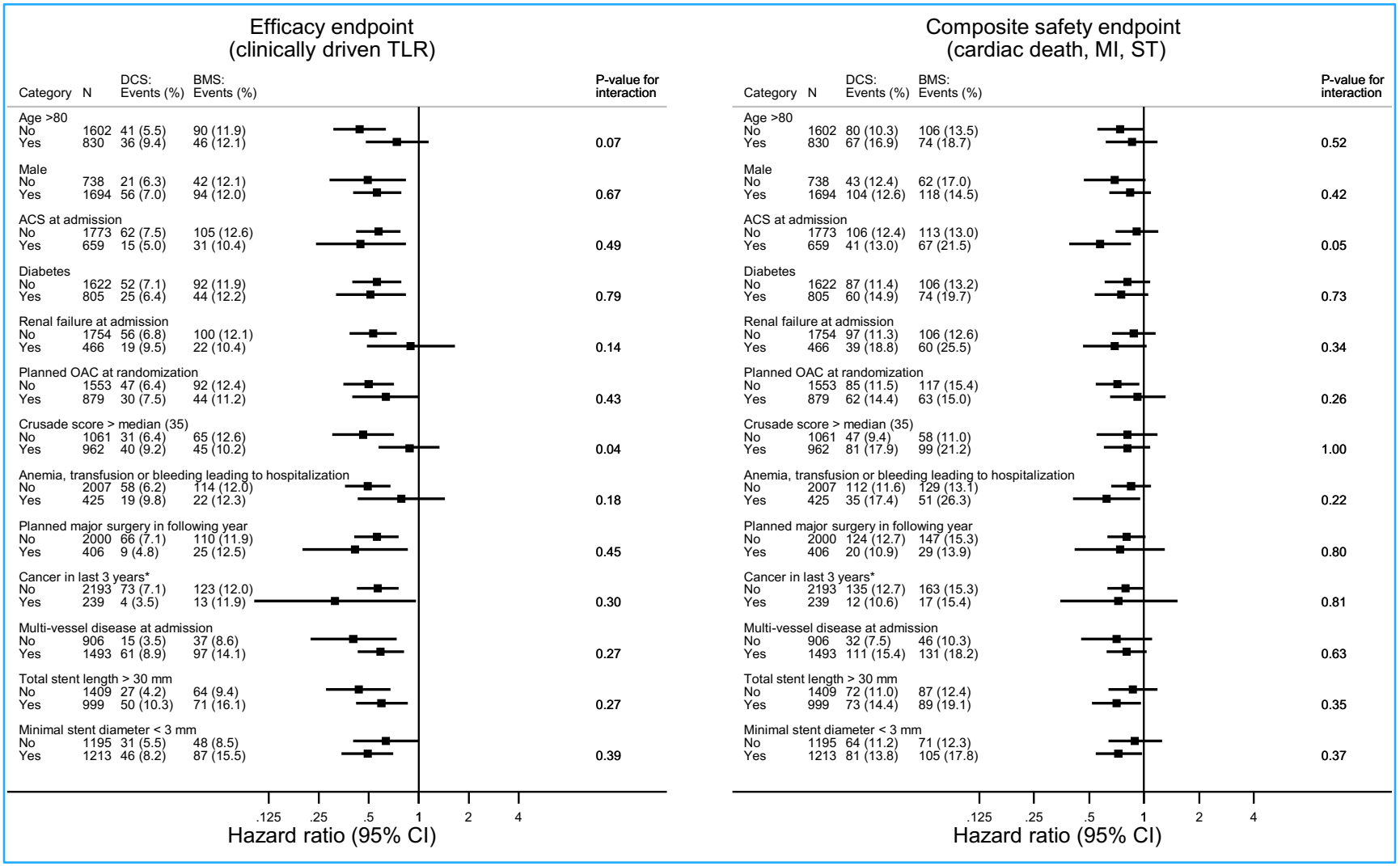


Number at Risk

DCS	1221	1129	1061	1013	626
BMS	1211	1074	999	945	561

2 year FU was obtained at 730 days ± 60 days

Subgroups at 2 years follow-up



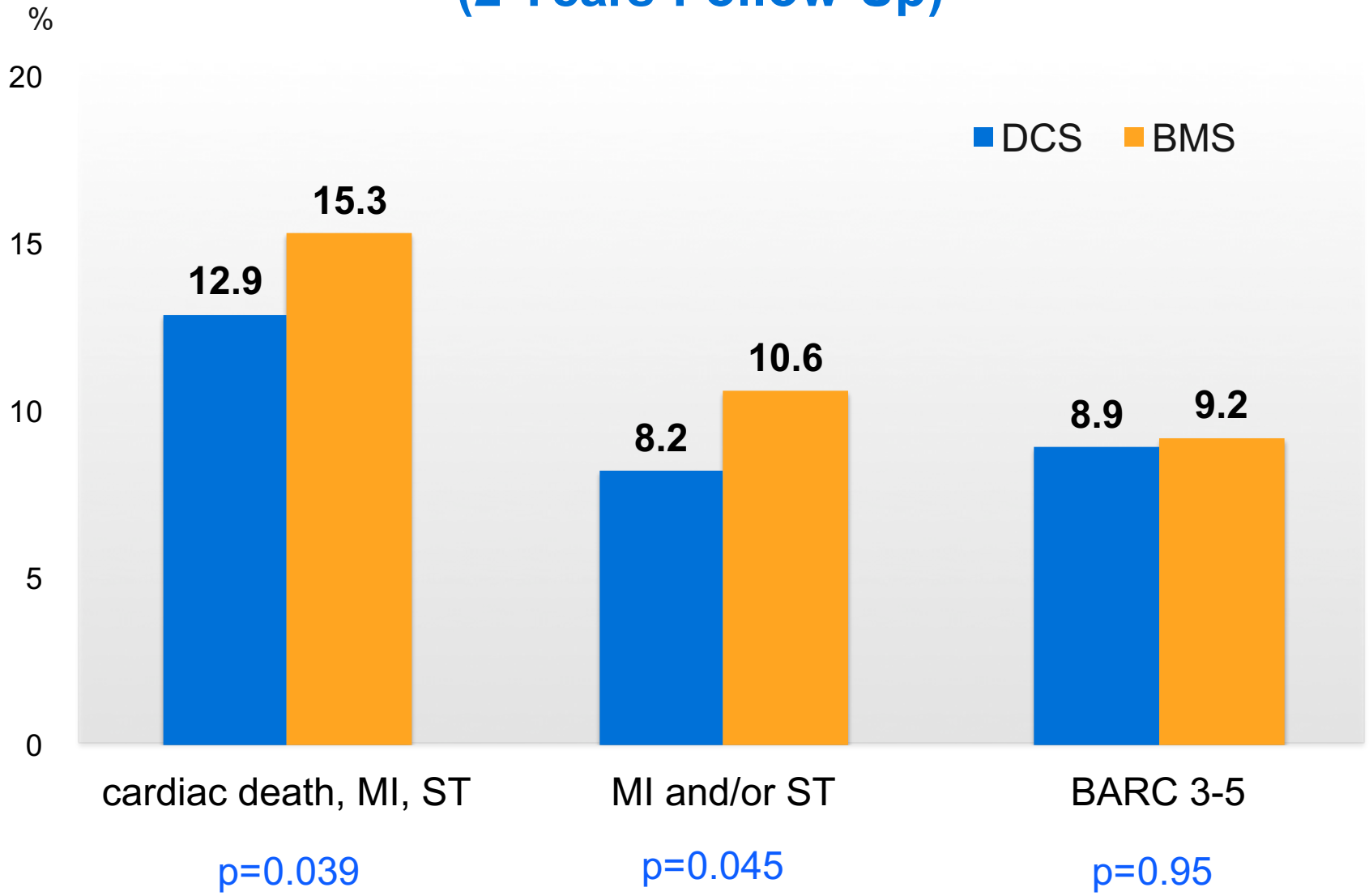
The Balance of Thrombosis and Bleeding

Multivariate Predictors of Primary Safety Endpoint and Major Bleeding (BARC 3-5)

	Cardiac death/MI/ST	Major Bleeding
Congestive heart failure	1.61 (1.23-2.11) p=0.001	
Multivessel disease	1.66 (1.27–2.18) p<0.001	-
Number of stents / patient (per stent)	1.20 (1.09–1.32) p<0.001	-
BMS (vs. DCS)	1.28 (1.03–1.59) p=0.027	-
Age > 75	1.56 (1.23–1.97) p<0.001	1.52 (1.13–2.06) p=0.006
Haemoglobin (per 1 mmol/l lower)*	1.32 (1.19–1.46) p<0.001	1.73 (1.52–1.96) p<0.001
Serum creatinine > 150 umol/l	-	1.58 (1.10–2.27) p=0.012
Planned oral anticoagulants	-	2.01 (1.51–2.68) p<0.001

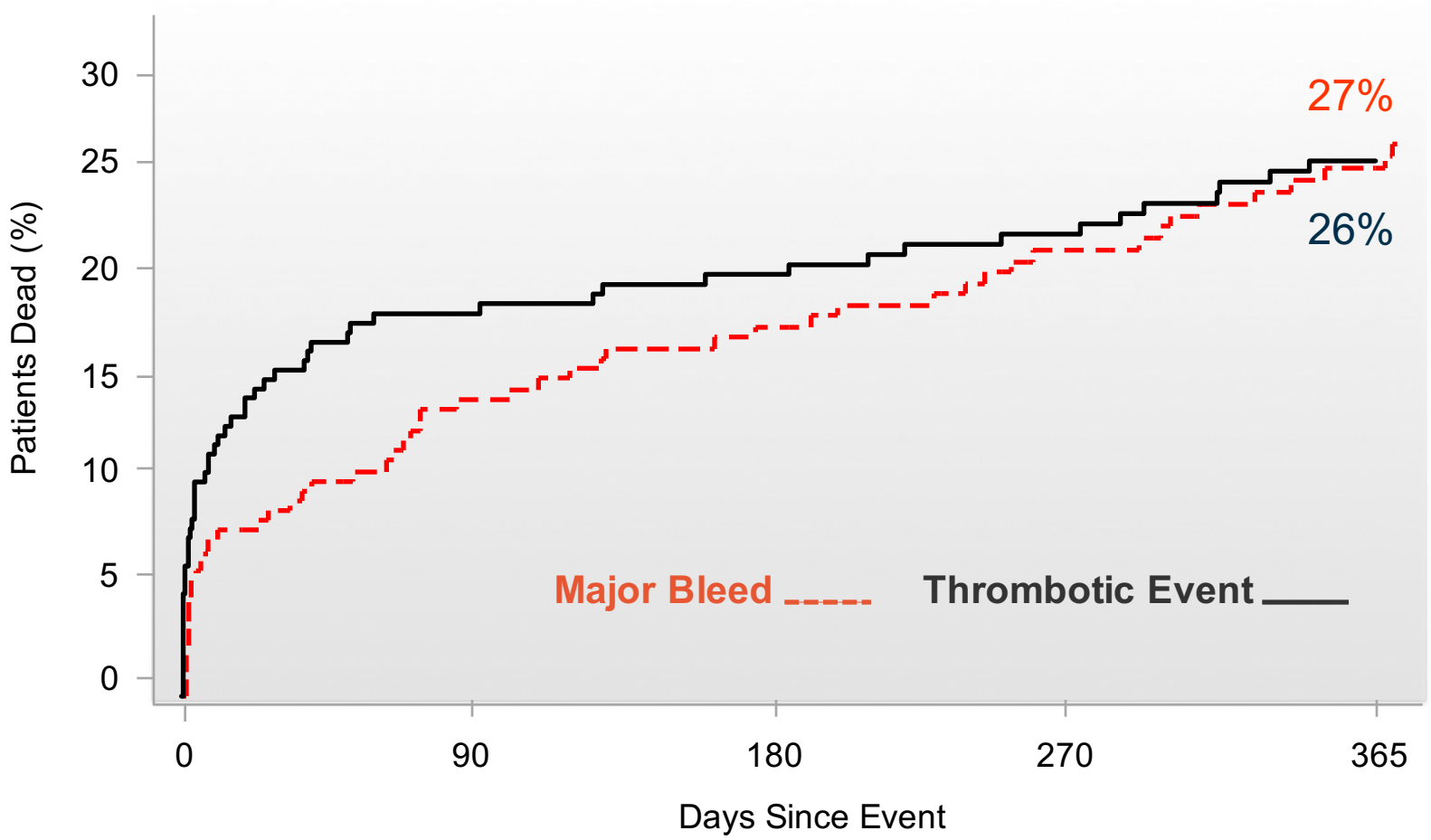
* Below 9 mmol/l (145 g/l)

Cardiac, Coronary and Major Bleeding events
(2 Years Follow-Up)



All % derived from Kaplan-Meier estimates

Mortality During the Year Following a Coronary Thrombotic Event (MI and/or ST) or a Major Bleeding event (BARC 3-5)



1-year mortality = 6% for patients with neither thrombotic nor major bleeding events

Conclusions

- ✓ At two years, the use of a BA9-DCS remained both significantly safer and more effective than a control BMS in HBR patients treated with a one-month only DAPT course
- ✓ No subgroup was identified for which use of a BMS was superior to a DCS
- ✓ HBR patients suffer from a persistently high incidence of bleeding and thrombotic events, both of which are associated with a high and similar mortality over a one year period
- ✓ Identification of predictors of both the composite primary safety event and major bleeding may help design future trials of DAPT duration for HBR patients