

# From LEADERS to LEADERS FREE

## A patient-centric approach

HBR Patients & 1 Month DAPT  
A Paradigm Shift With LEADERS FREE

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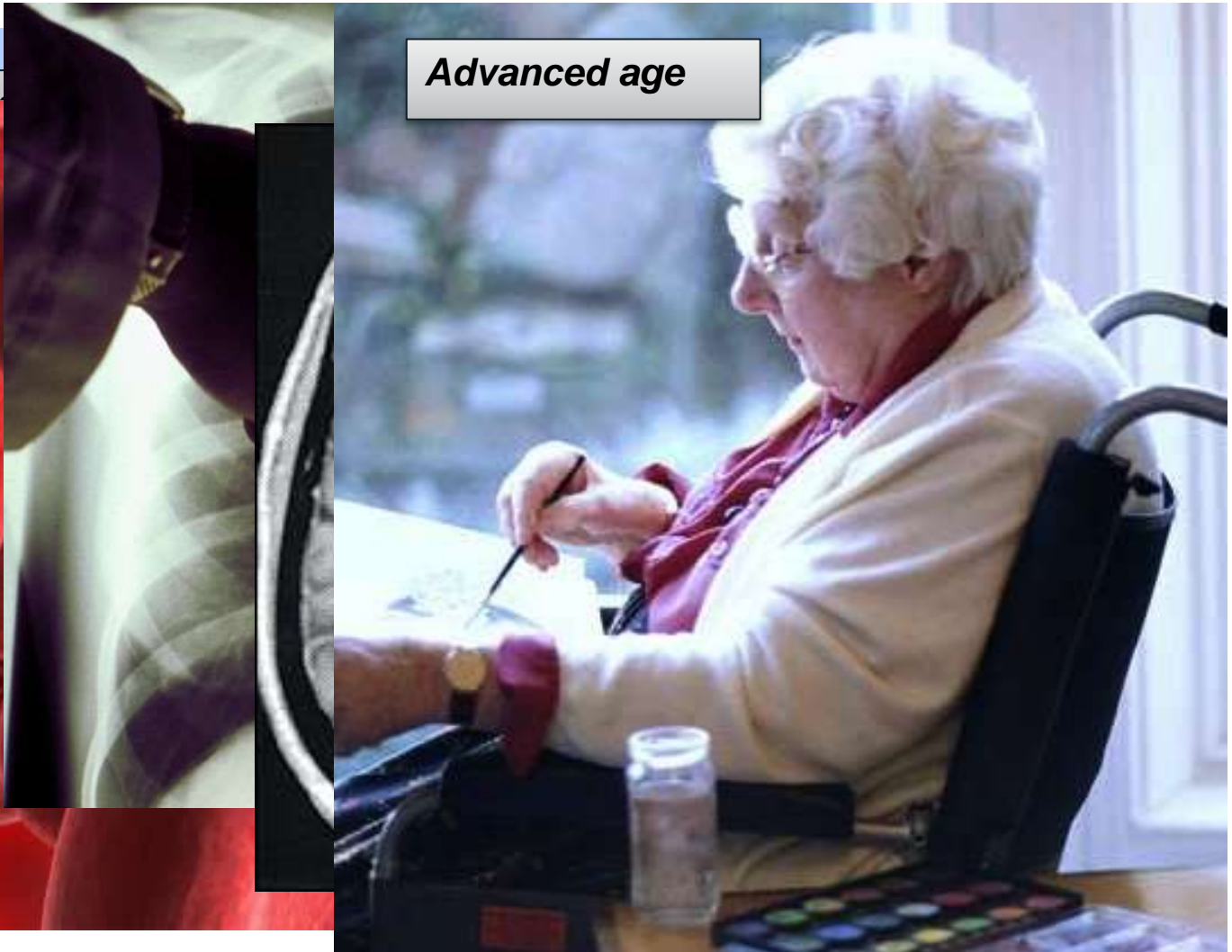
21<sup>st</sup> CardioVascular Summit  
**TCTAP 2016**

LEADERS FREE

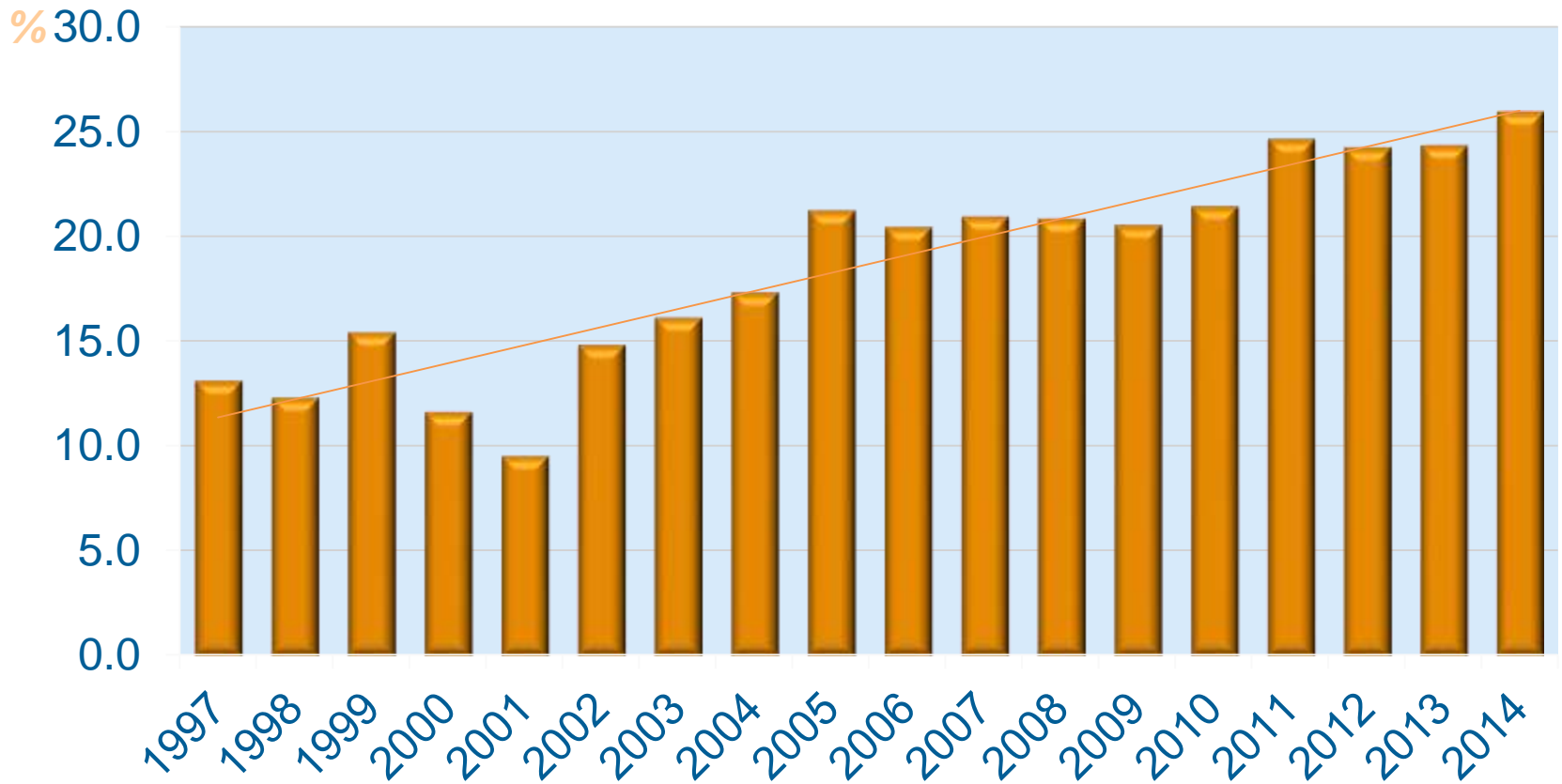
# High Bleeding Risk Patients (HBR)

*Need for anti*

*Advanced age*

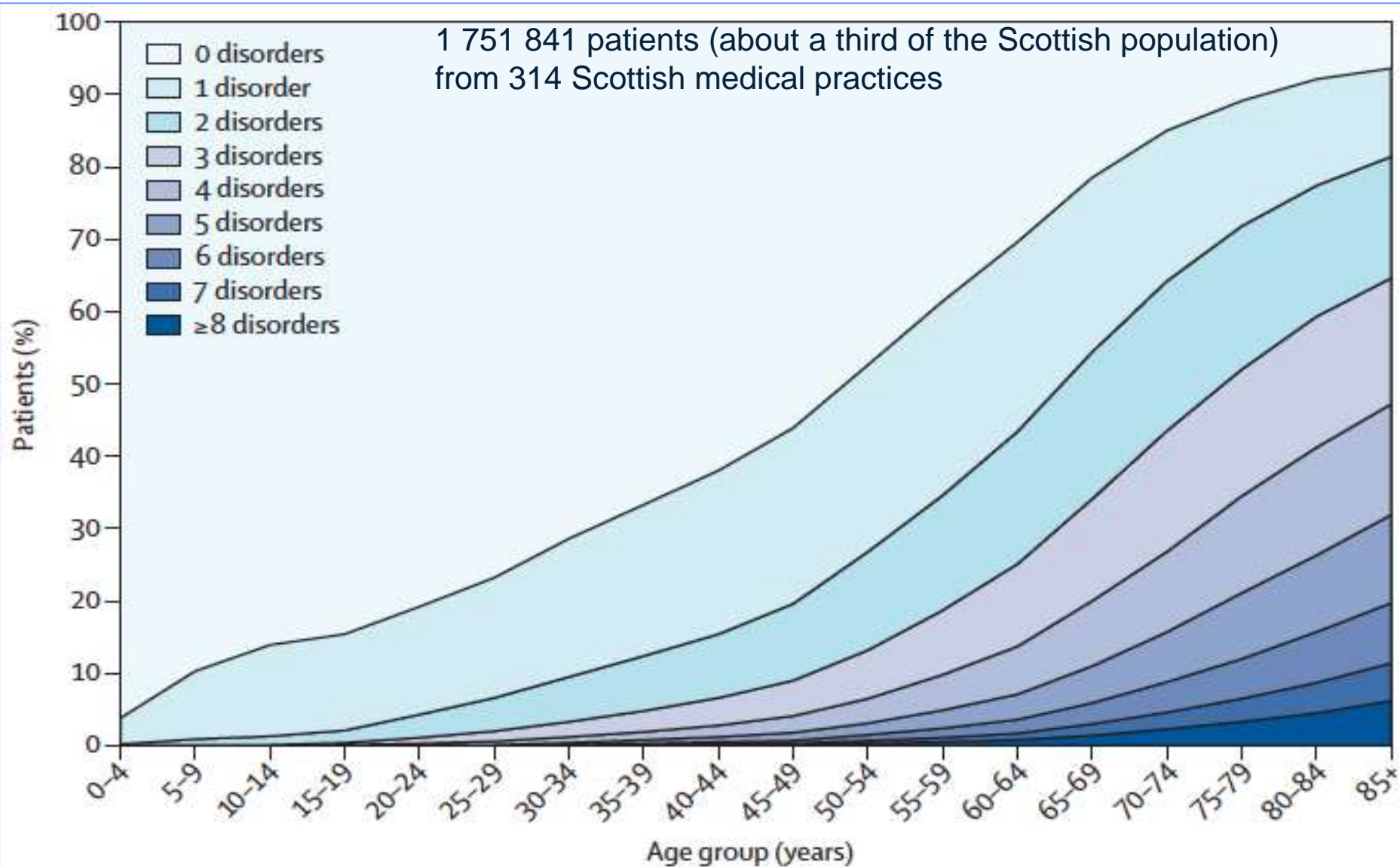


# ACS patients $\geq 75$ years, who underwent PCI (n=33,834)



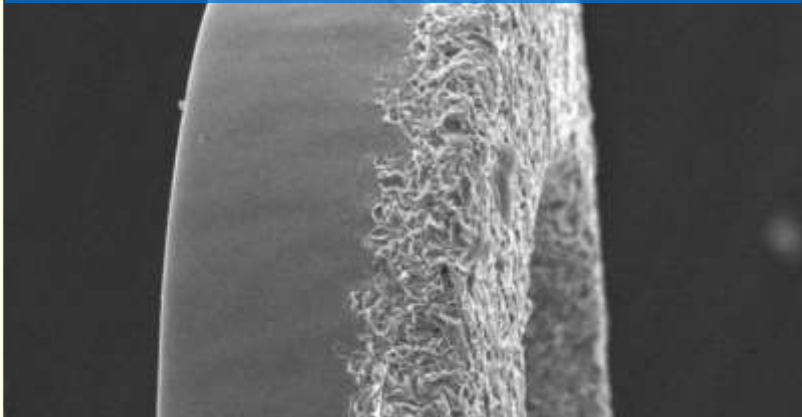
# Number of chronic disorders by age-group

*Barnett K et al. Lancet 2012; 380: 37-43*

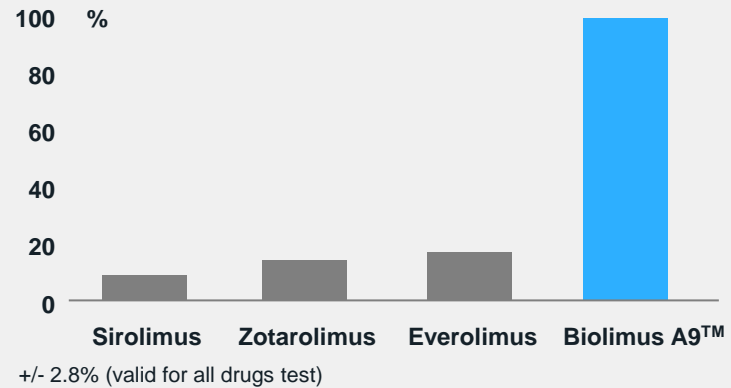


# BioFreedom™ Drug Coated Stent (DCS)

Selectively Micro-Structured Surface Holds Drug in Abluminal Surface Structures



BA9™ Drug 10 Times More Lipophilic than Sirolimus<sup>1</sup>



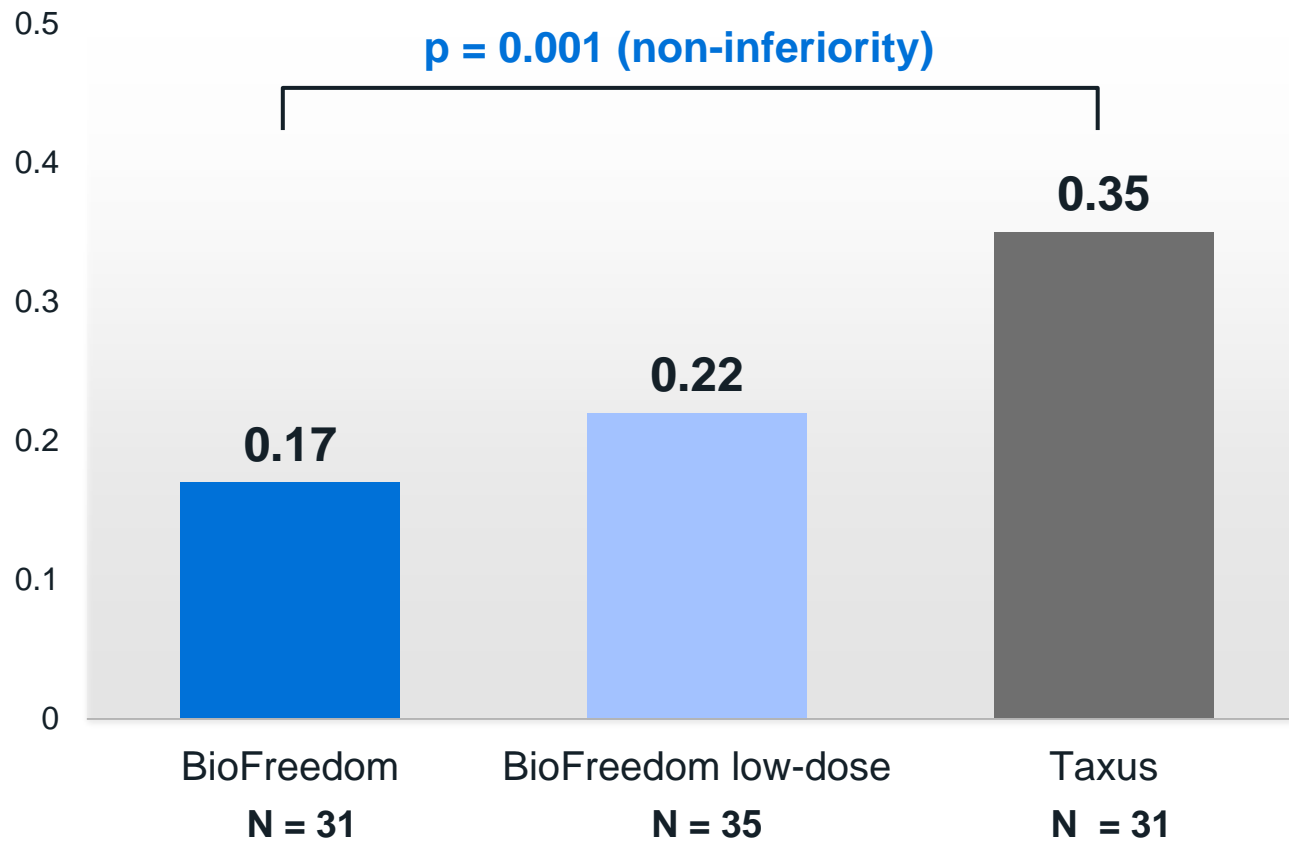
## Potential Advantages:

- ✓ Avoid any possible polymer-related adverse effects
- ✓ Rapid drug transfer to vessel wall (98% within one month<sup>2</sup>)
- ✓ Safe to shorten DAPT?

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

# Median In-Stent LLL at 12-month Follow-up

## 2<sup>nd</sup> Cohort – Primary Endpoint



# LEADERS FREE Trial Design

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

**BioFreedom™  
DCS**

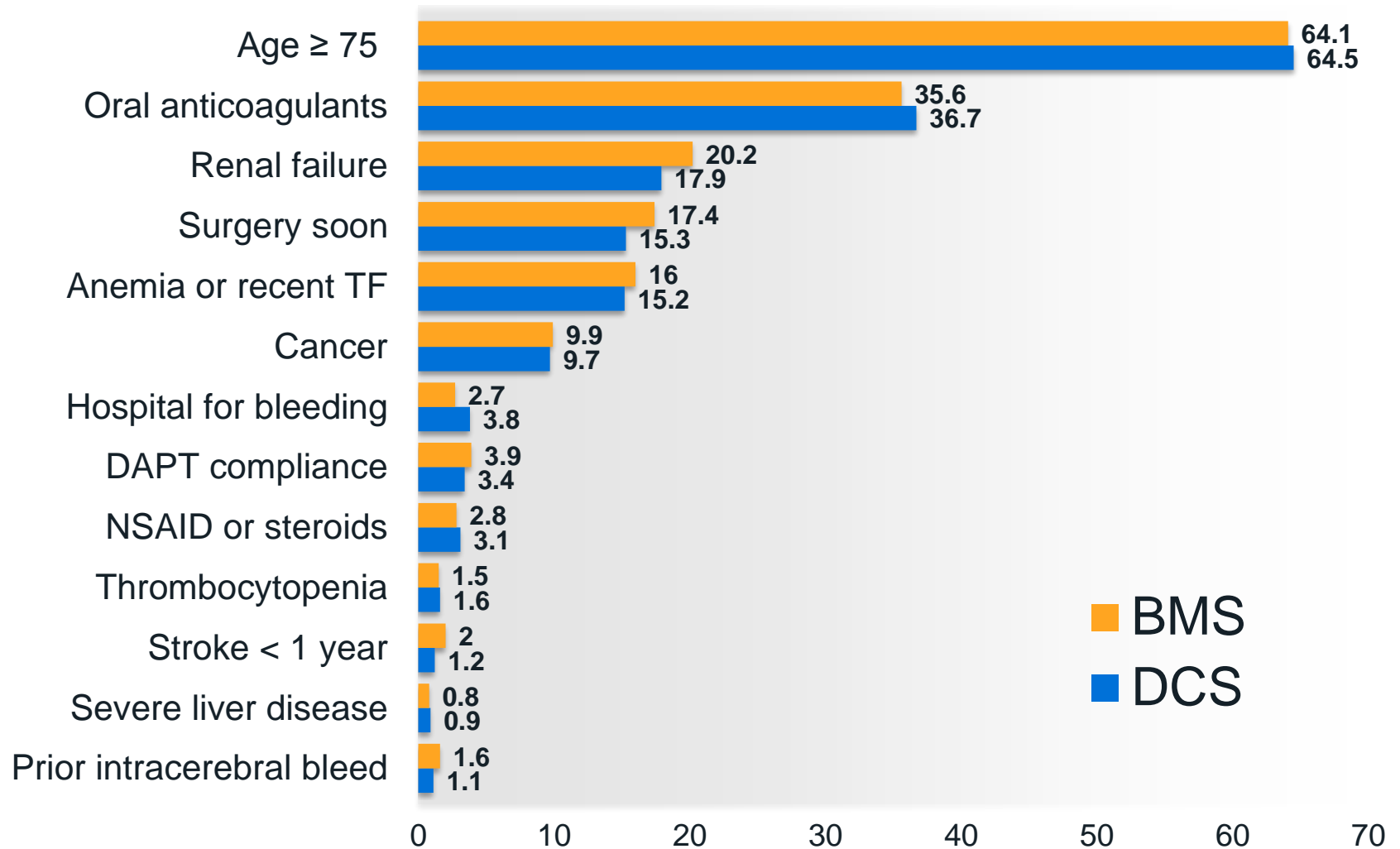
**vs.**

**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)

# Inclusion Criteria Applied (1.7 criteria / patient)



■ BMS  
■ DCS



# Baseline Characteristics

	DCS (%)	BMS (%)
→ Mean age	75.7 + 9.4	75.7+9.3
Female gender	29.8	30.9
BMI	27.5 ± 4.8	27.2 ± 4.6
→ Diabetes	34.0	32.3
NSTEMI presentation	22.4	23.2
STEMI presentation	4.7	4.0
Prior MI	19.6	21.4
Prior PCI	22.2	21.9
Prior CABG	9.4	10.1
→ Multivessel CAD	62.9	61.6
Congestive heart failure	14.4	12.4
→ Atrial fibrillation	34.9	34.6
Peripheral vascular disease	15.7	15.8
Chronic obstructive lung disease	10.9	11.7

None of the baseline characteristics differ at p < 0.05

# Index Procedure

	DCS (%)	BMS (%)
➔ Radial access	60.7	58.7
Staged procedure	4.5	5.9
Multi-lesion procedure	37.8	35.3
➔ Multi-vessel procedure	21.8	21.4
Number of treated lesions / patient	1.6 ± 0.8	1.6 ± 0.9
LMS	3.0	3.9
SVG	1.4	1.8
Bifurcation	14.9	16.0
ISR	2.4	2.6
CTO	5.0	4.4

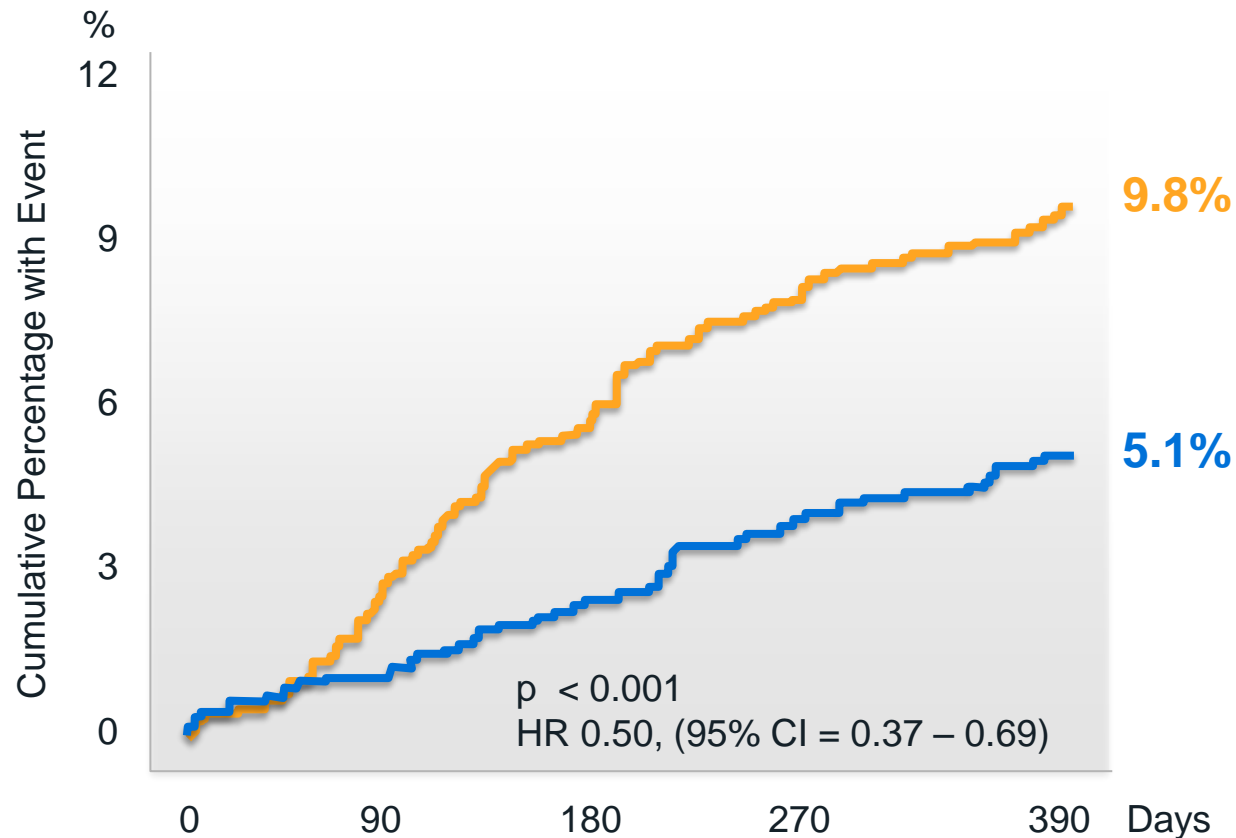
None of the procedure characteristics differ at  $p < 0.05$

# Index Procedure (Continued)

	DCS	BMS
Mean stent diameter	3.0 ± 0.4	3.0 ± 0.4
→ Mean total implanted stent length / patient	34.5 ± 23.1	33.4 ± 23.4
Mean number of stents implanted / patient	1.9 ± 1.1	1.8 ± 1.2
Lesion success	97.7	98.0
→ Device success	97.7	97.6
Procedure success	94.4	93.7
UFH during procedure	90.5	89.4
LMWH during procedure	8.4	8.8
Bivalirudin during procedure	1.1	1.8
2b3a blocker during procedure	2.0	1.2

None of the procedure characteristics differ at  $p < 0.05$

# Primary Efficacy Endpoint (Clinically-Driven TLR)

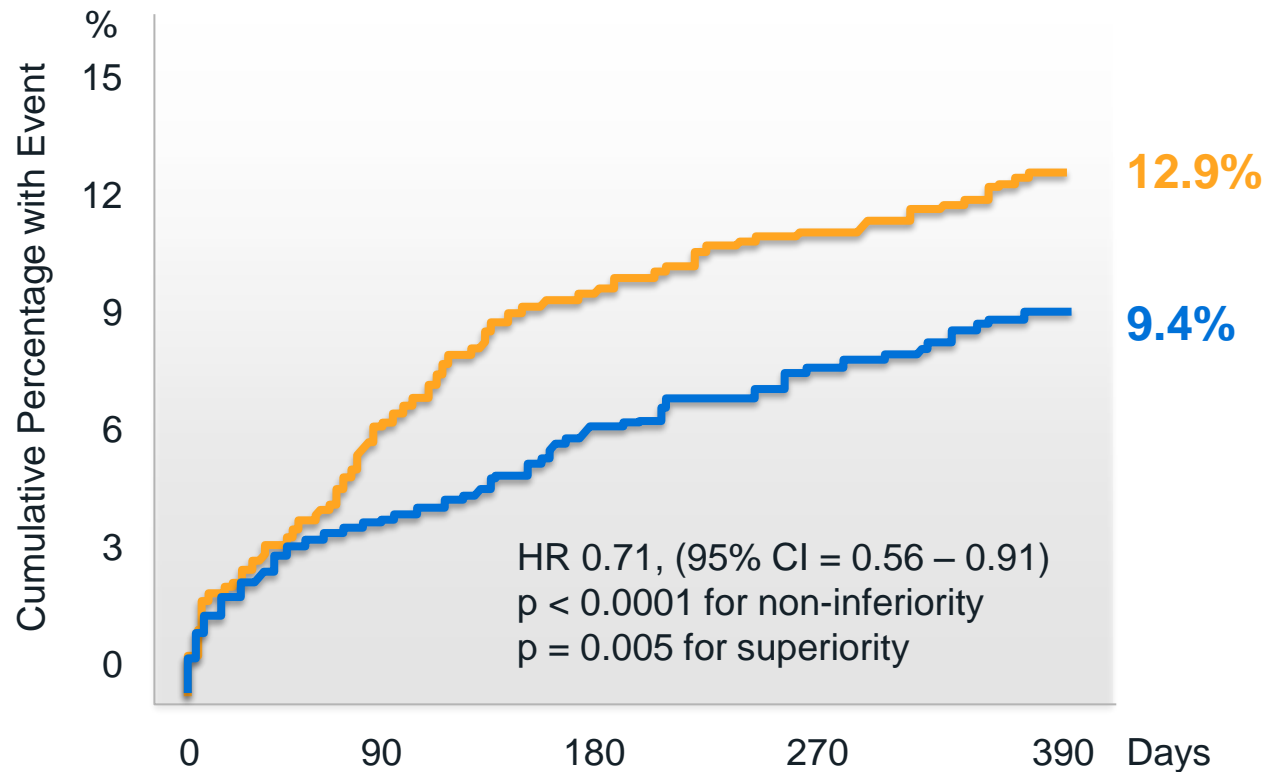


## Number at Risk

	0	90	180	270	390
DCS	1221	1167	1130	1098	1053
BMS	1211	1131	1072	1034	984

390 days chosen for assessing primary EP to capture potential events driven by the 360 day FU contact

# Primary Safety Endpoint (Cardiac Death, MI, ST)

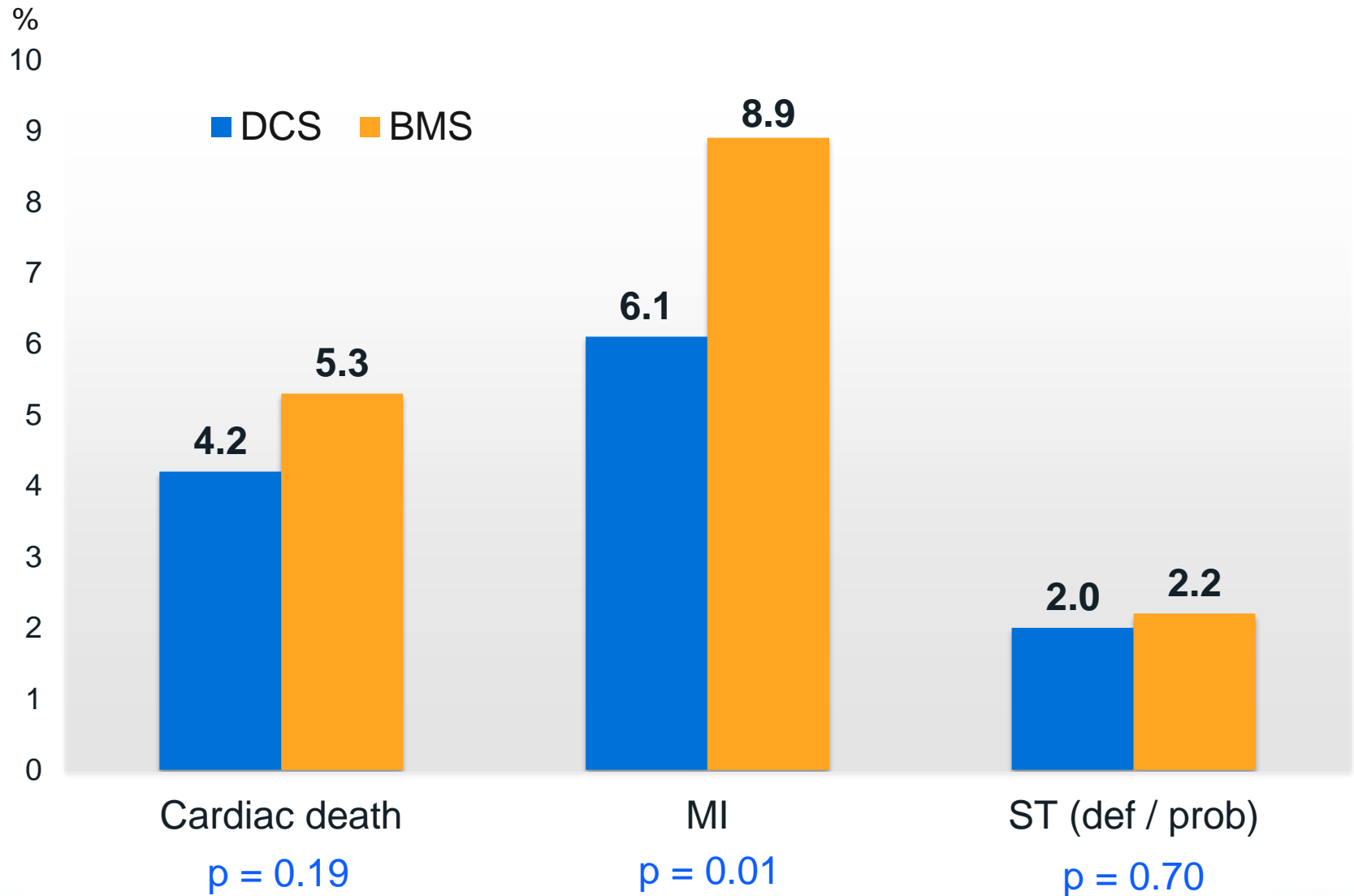


## Number at Risk

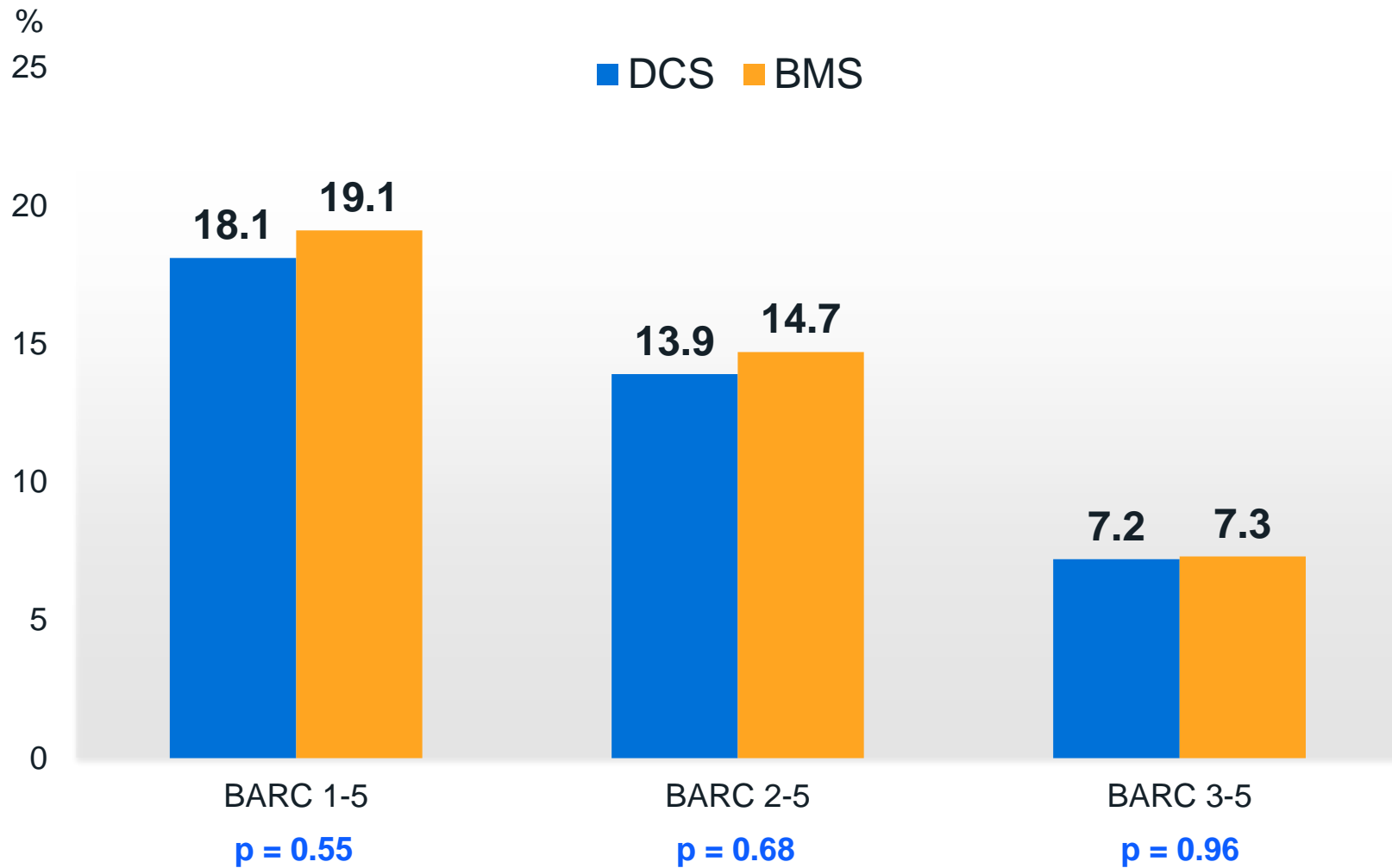
	0	90	180	270	390
DCS	1221	1146	1105	1081	1045
BMS	1211	1115	1066	1037	1000

390 days chosen for assessing primary EP to capture potential events driven by the 360 day FU contact

# Components of Safety Endpoint

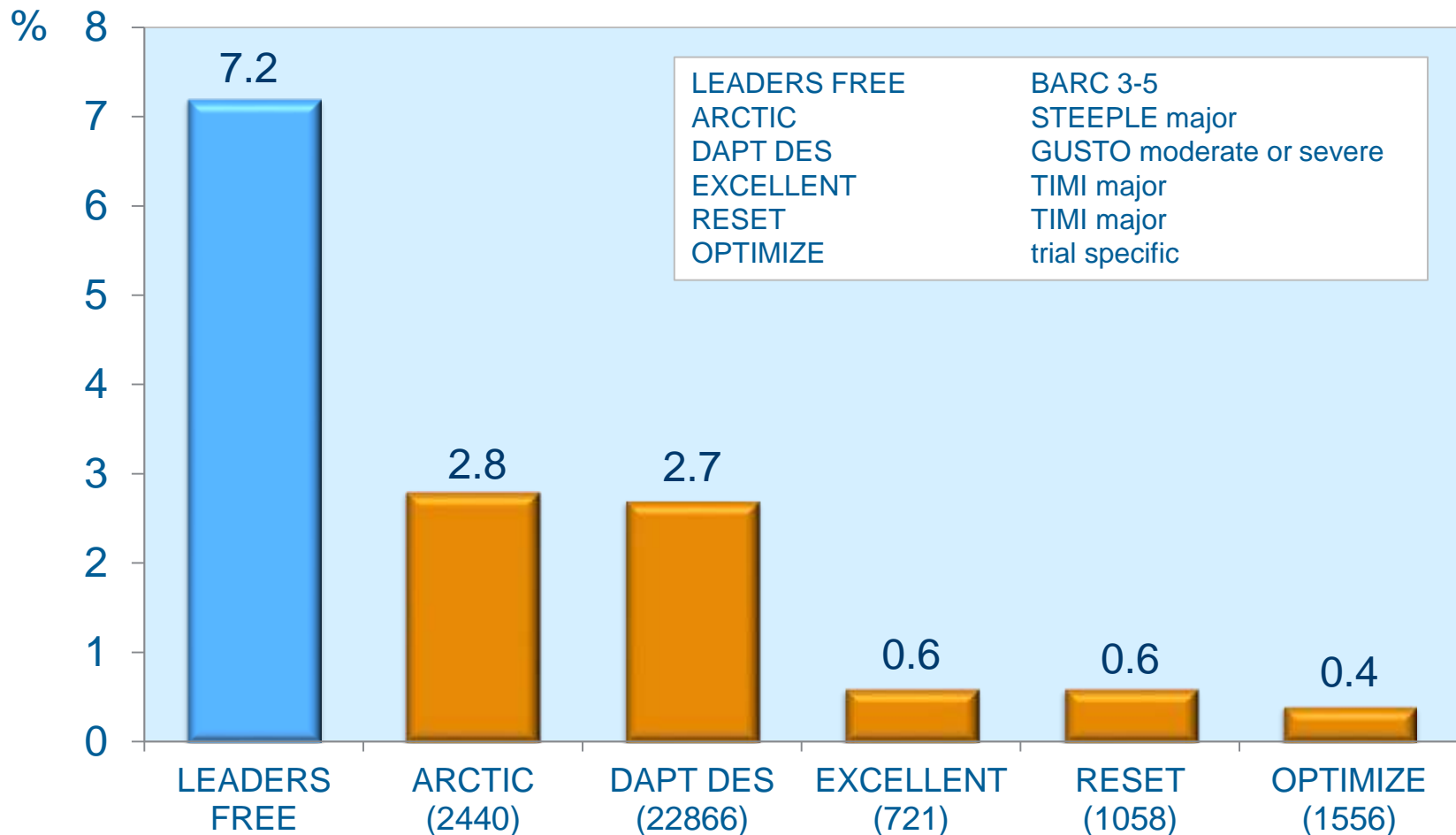


# Bleeding During 12 Months Follow-Up



# Major bleeding in DES DAPT trials

(first 12 months on DAPT after PCI)



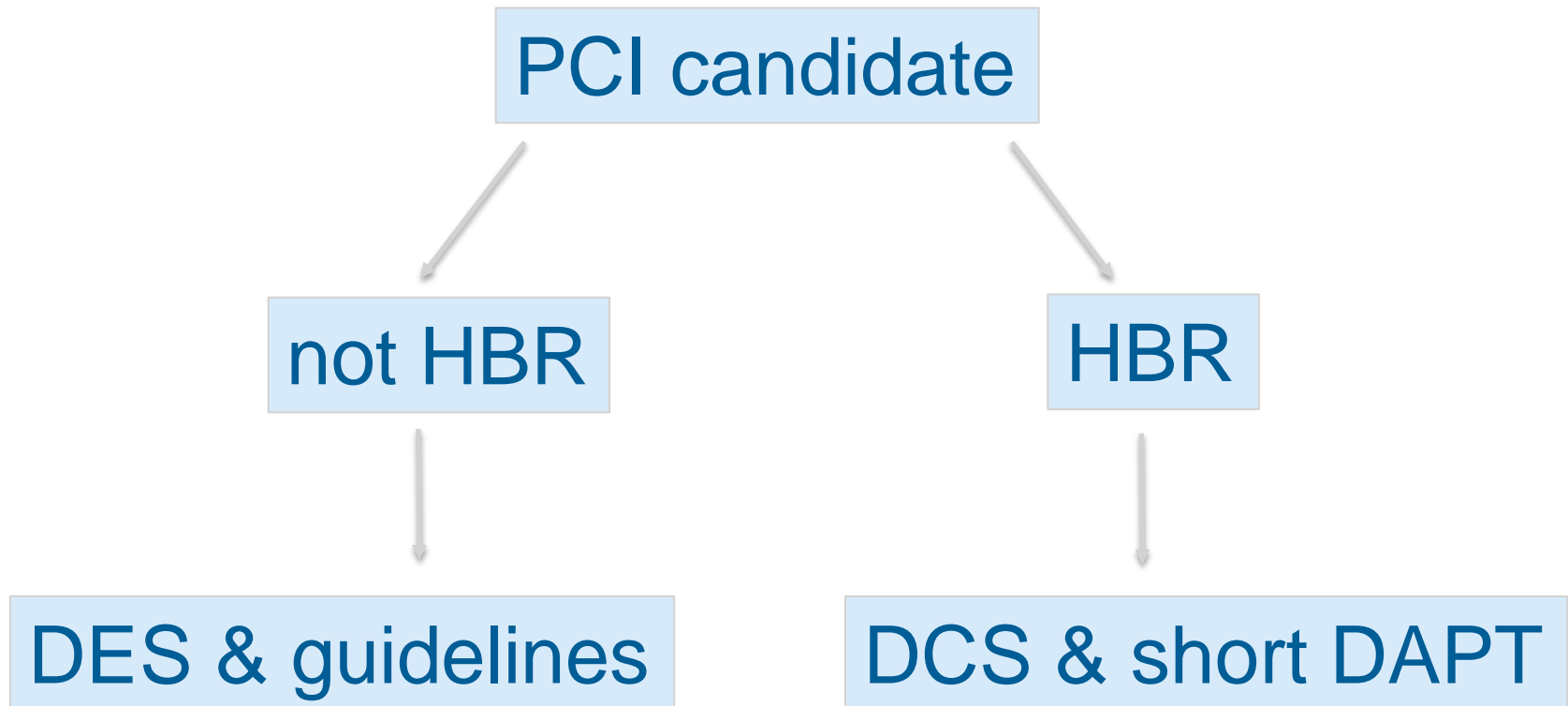


# DAPT trials exclusion criteria ( X )

# vs. LEADERS FREE inclusion criteria ( ✓ )

	EXCELLENT	RESET	ARCTIC	OPTIMIZE	DAPT DES	LEADERS FREE
Low Hb or thrombocytopenia	X	X	X			✓
Recent bleeding	X	X	X			✓
Anticoagulants	X		X		X	✓
Need for surgery	X		X	X	X	✓
Renal or hepatic failure	X	X	X			✓
STEMI and/or GP 2b3a blockers	X		X	X		not excluded
Anticipated difficulties with long term DAPT	X	X	X		X	✓

There now is a choice...



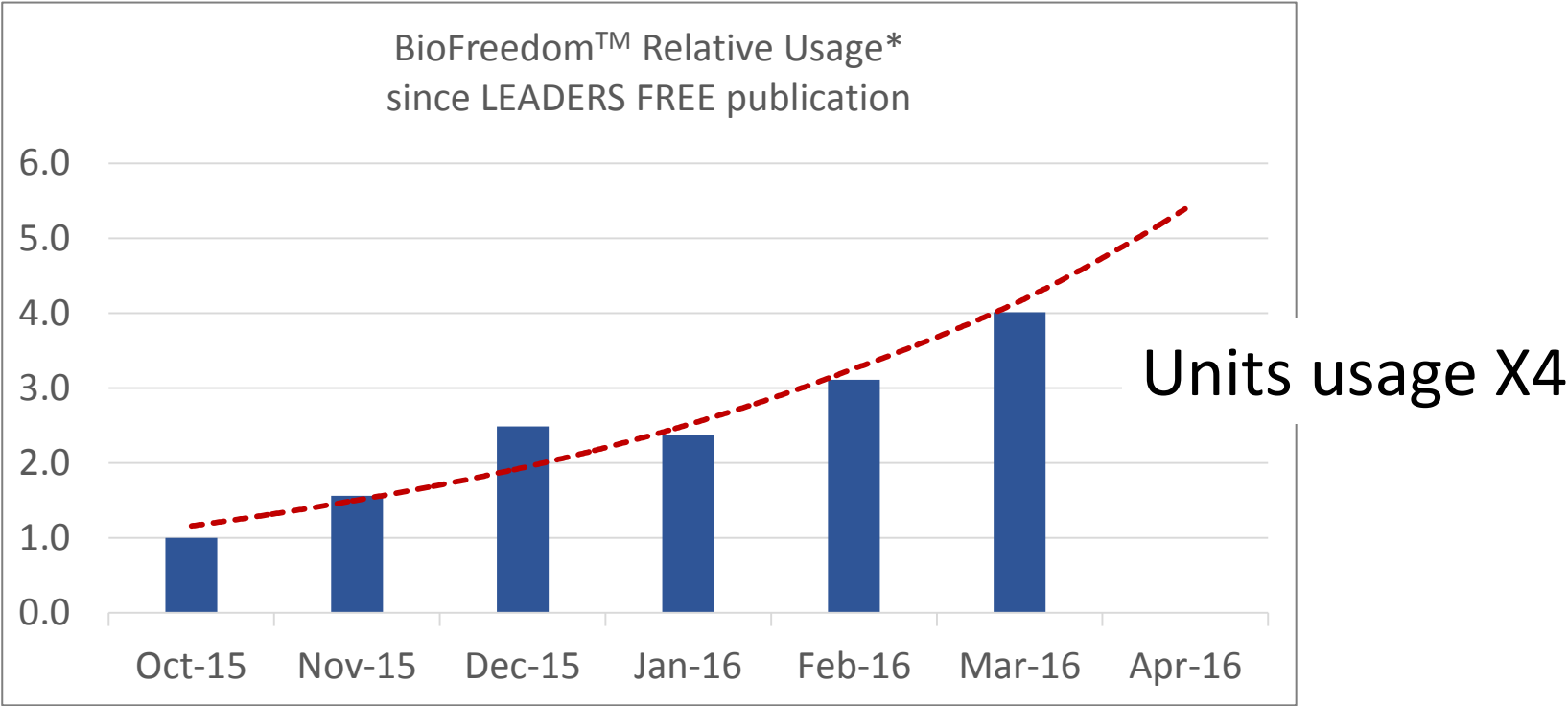
# Novel Ticagrelor regimens

	<b>PEGASUS</b>	<b>GLOBAL LEADERS</b>	<b>TWILIGHT</b>
Number of patients	21162	16000	9000
Status	published	enrolling	enrolling
Patients	Post-MI	All-comers PCI	High-risk PCI
Design	ASA alone vs. ASA+ticagrelor 60 mg or ticagrelor 90 mg BD	1 mth DAPT (ASA), then ticagrelor monotherapy vs. Guideline-recommended DAPT	3 mths DAPT (ticagrelor + ASA), then continued DAPT vs. ticagrelor alone
Randomization	stat	at PCI	3 months post PCI
Ticagrelor Rx.	3 years	2 years	15 months
Primary endpoint	Cardiovasc. death, MI or stroke (✓)	All-cause mortality or Q wave MI	Bleeding
<b>HBR excluded</b>	<b>yes</b>	<b>yes</b>	<b>yes</b>

## Exclusion ( ✗ ) vs. inclusion ( ✓ ) criteria

	PEGASUS	GLOBAL LEADERS	TWILIGHT	LEADERS FREE
Anticoagulants	✗	✗	✗	✓
Cancer			✗	✓
Recent bleed/diathesis	✗	✗		✓
Major surgery soon		✗	✗	✓
AMI presentation	✗		✗	not excluded
Severe liver disease	✗	✗	✗	✓
Thrombopenia			✗	✓
Recent CVA	✗	✗	✗	✓
Any ICH	✗	✗	✗	✓
Use of CYP3a4 inhibitor		✗	✗	not excluded
Risk of bradycardic event	✗			not excluded

# BioFreedom™ DCS Adoption\* since LEADERS FREE Publication



\*Relative units usage compared to October usage (Biosensors internal data, April 2016)

# Conclusions (I)

- ✓ LEADERS FREE is the first randomized clinical trial dedicated to HBR patients
- ✓ Such patients are often excluded from stent and drug trials, constitute a rapidly growing proportion of PCI candidates and suffer high event rates
- ✓ Together with an ultra-short (1 month) DAPT course, the use of a BA9-DCS was both significantly safer and more effective than a control BMS in HBR patients

# Conclusions (II)

- ✓ Most major trials of antiplatelet regimens and devices have targeted specific populations: it is probably inappropriate to extend their conclusions to HBR patients
- ✓ The BioFreedom DCS with 1 month DAPT should be considered as the current default therapy for HBR patients
- ✓ Use of BMS can only be justified today for economic reasons

# Late-breaking at Euro PCR 2016

- LEADERS-FREE ACS

Christoph Naber

- The Balance of thrombosis and bleeding in the LEADERS FREE trial

Philip Urban



Thank you