LEADERS-FREE

Which DES in High Bleeding Risk Patients?

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Hôpital de la Tour
Geneva Switzerland

Recent Late-Breaking Trials – Clinical Implications

21st CardioVascular Summit
TCTAP 2016

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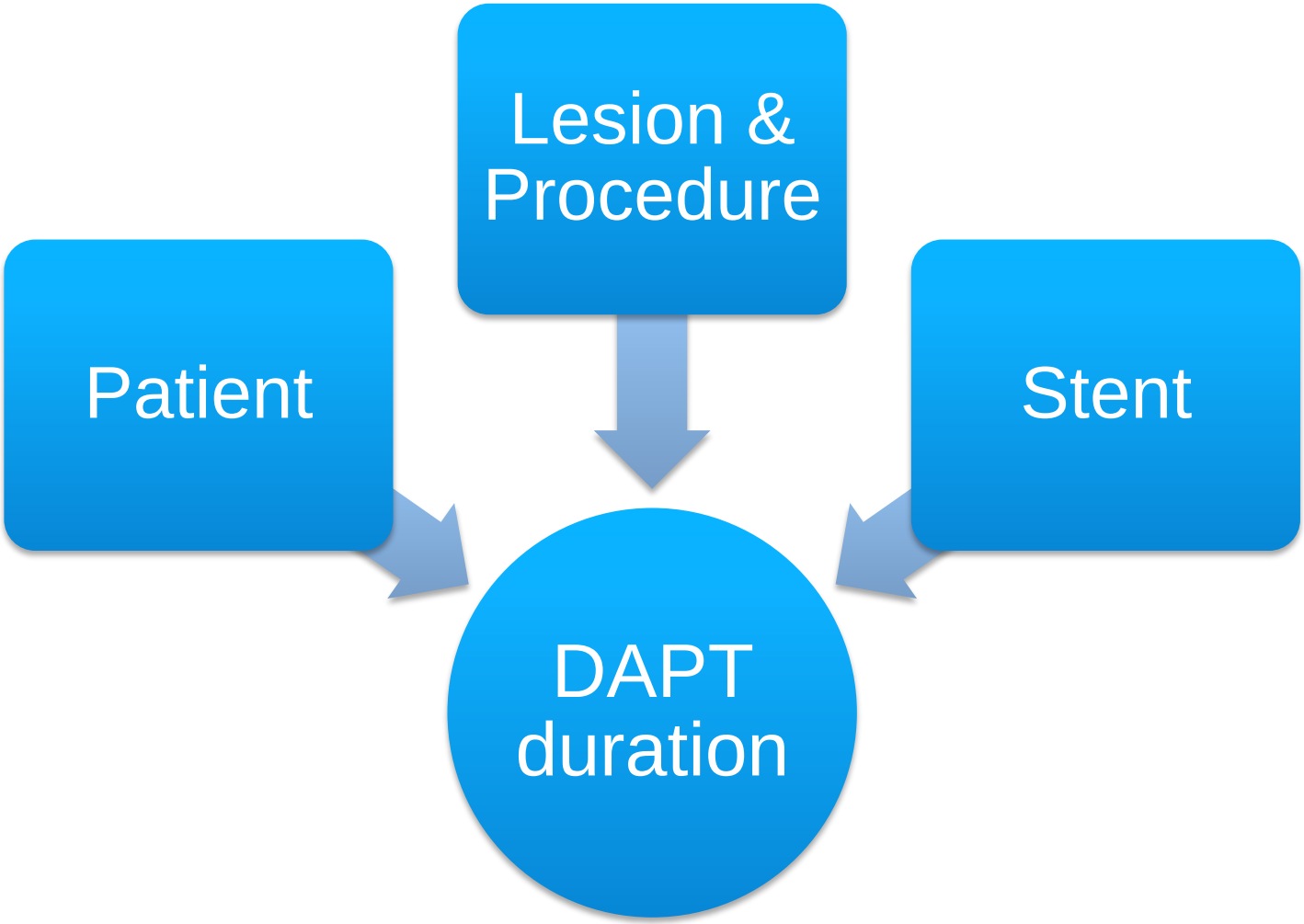
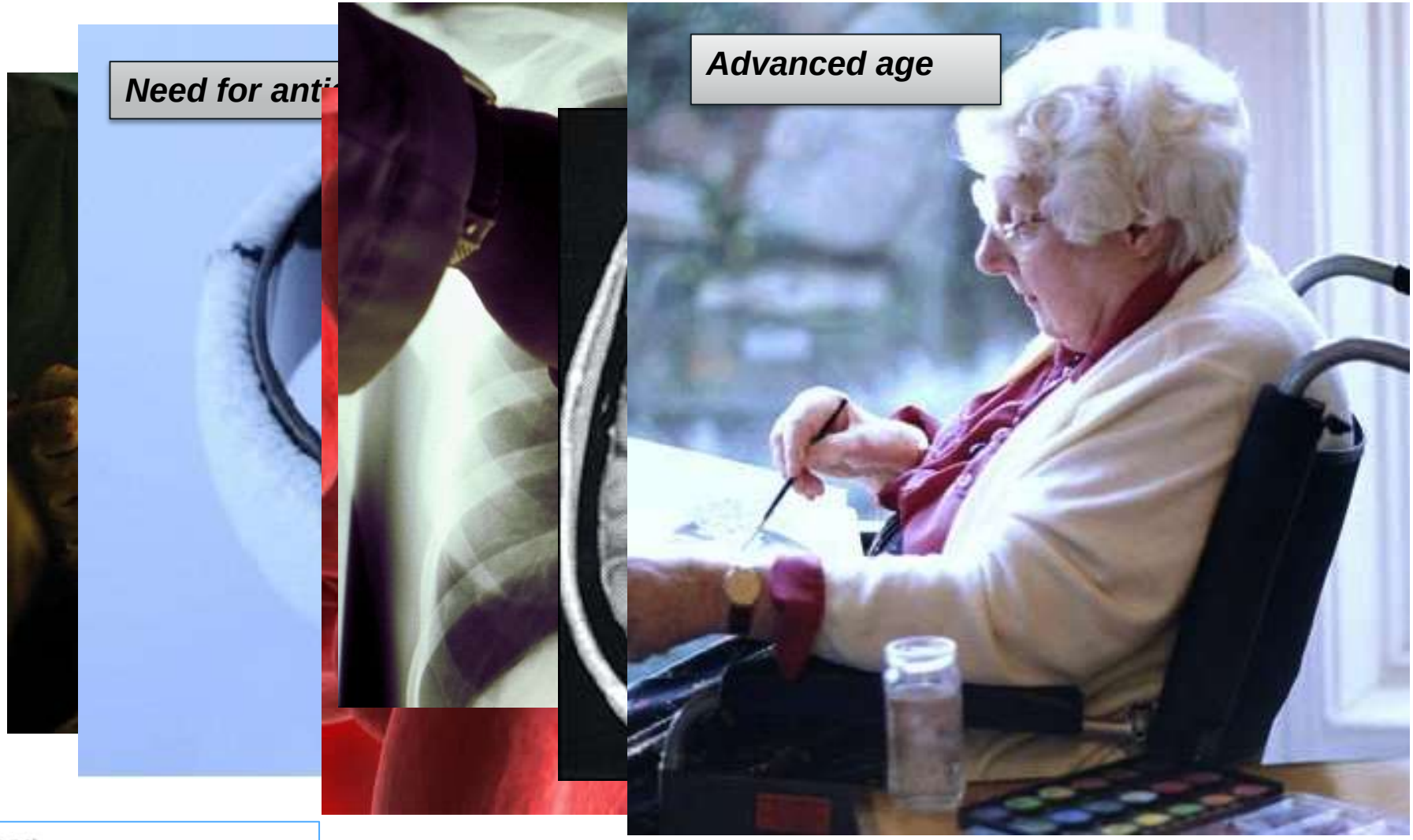
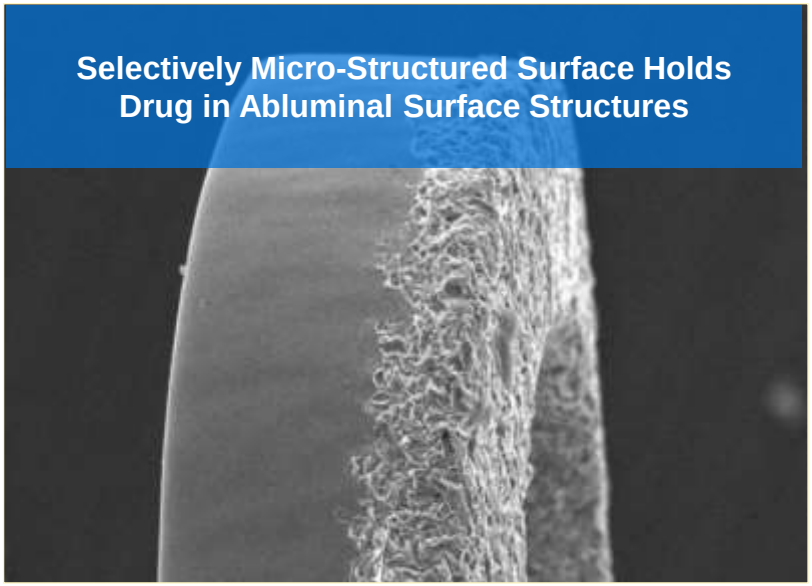
Optimal DAPT duration after coronary stenting?

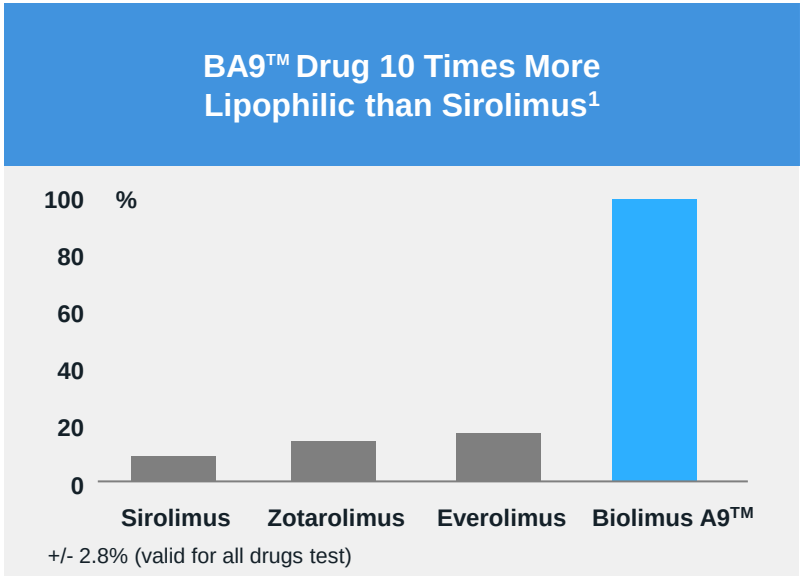

Lesion &
Procedure
Patient
Stent
DAPT
duration

High Bleeding Risk Patients (HBR)



BioFreedom™ Drug Coated Stent (DCS)





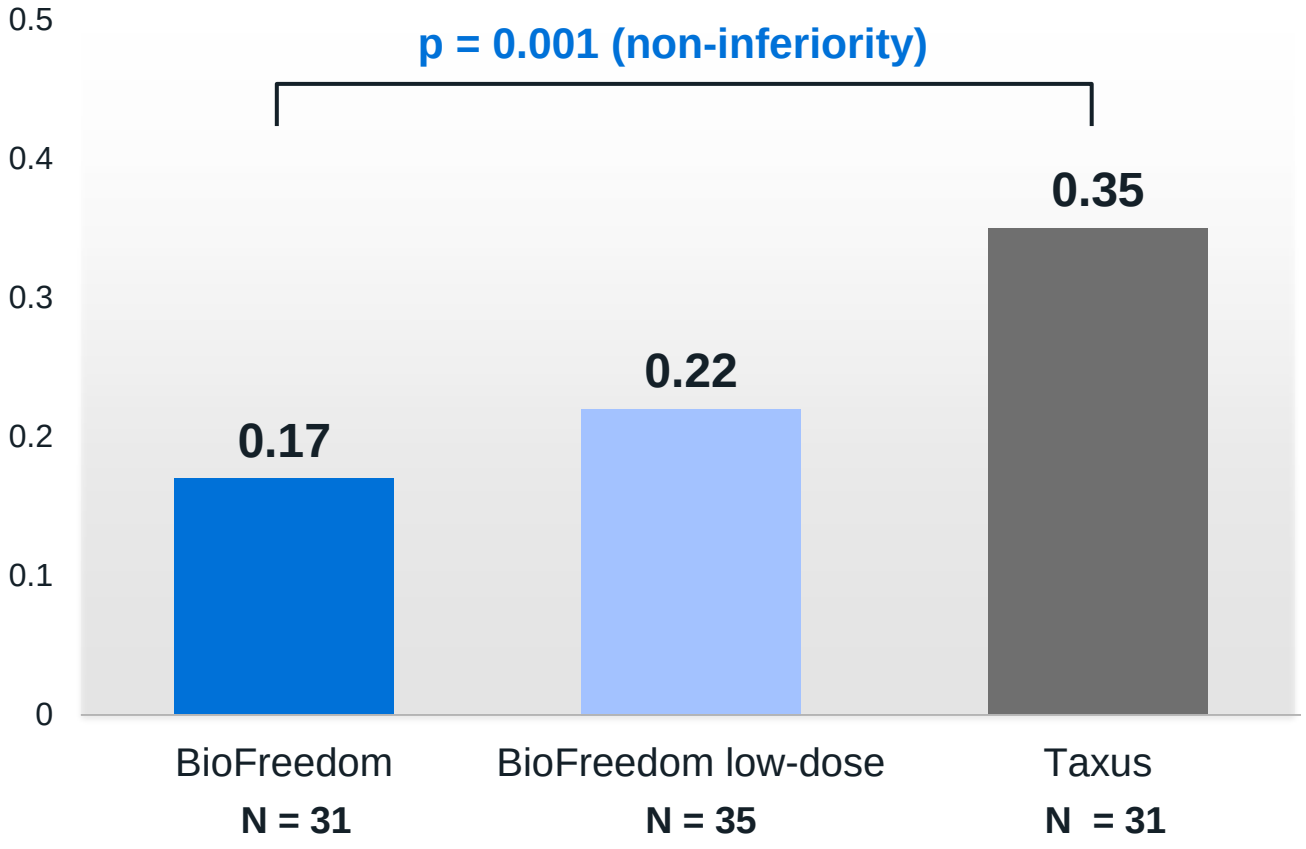
Potential Advantages:

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

2nd Cohort – Primary Endpoint



Costa R et al. J Am Coll Cardiol Intv. 2016; 9: 51-64

LEADERS FREE Trial Design

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

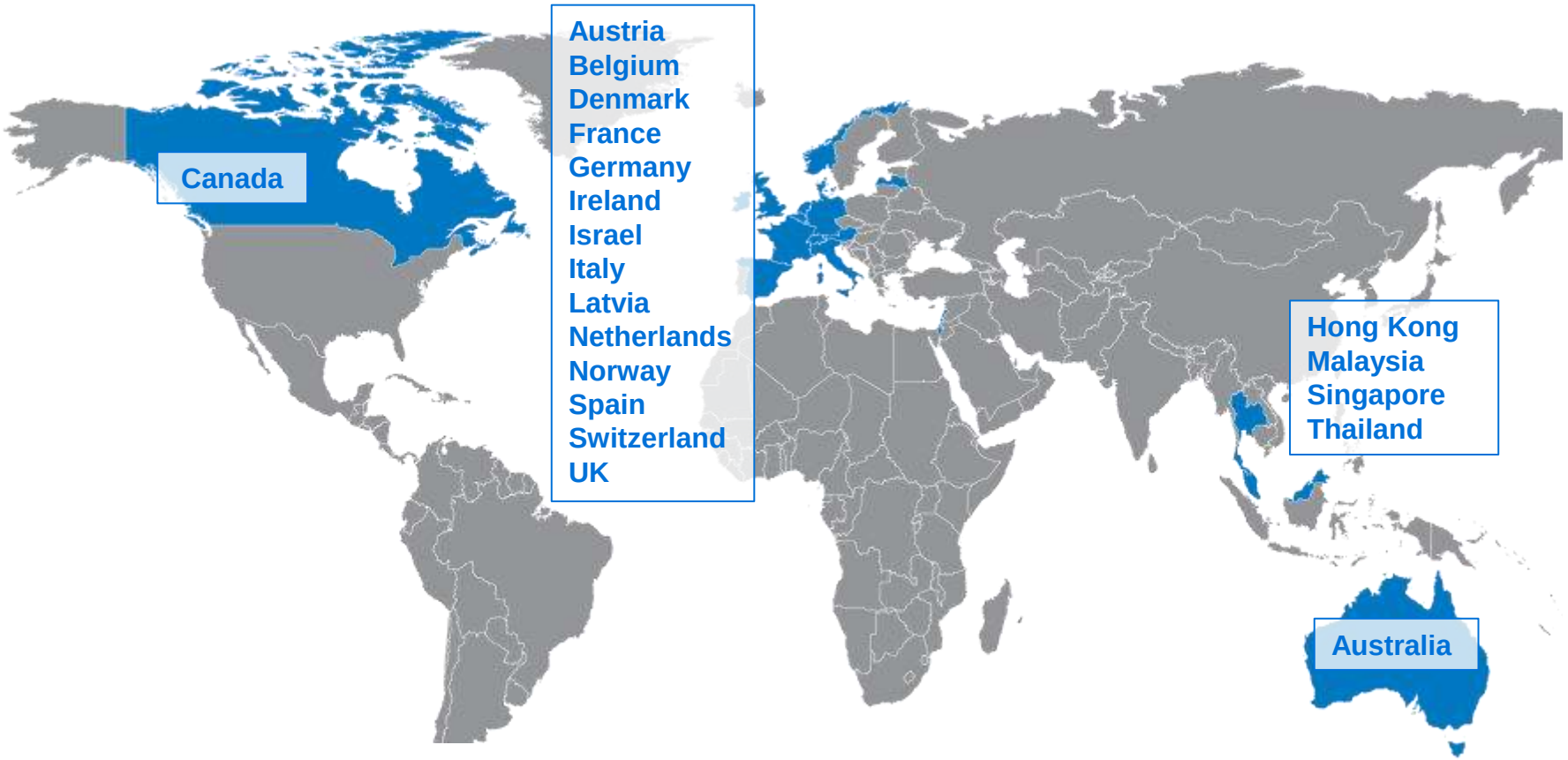
BioFreedom™ DCS	vs.	Gazelle™ BMS

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)

Urban P et al. Am Heart J 2013; 165: 704-9

20 Participating Countries



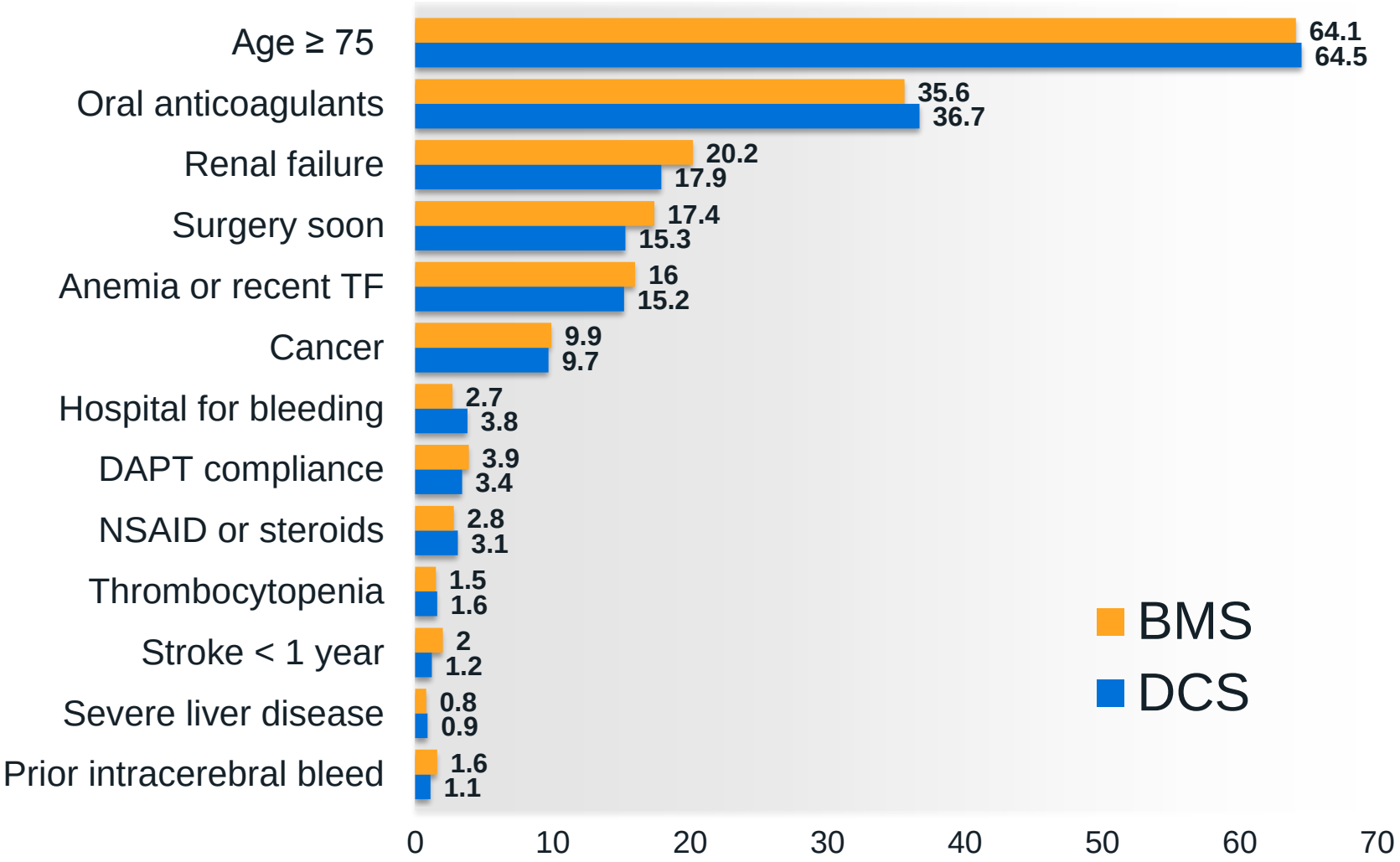
2466 Patients

Enrolled December 2012–May 2014

Leaders Free – Asian & Australian Centers

Participating Center	Principal Investigator	Enrollment
Tan Tock Seng Hospital, SG	Paul Ong	41
Queen Mary Hospital, HK	Stephen Lee	35
National Hear Institute, MY	Robaayah Zambahari	31
Siriraj Hospital, TH	Damras Tresukosol	30
National Heart Centre Singapore, SG	LIM Soo Teik	19
MonashHeart, AU	Ian Meredith	17
The Prince Charles Hospital, AU	Darren Walters	14
National University Health System, SG	Chan Koo Hui	7

Inclusion Criteria Applied (1.7 criteria / patient)



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

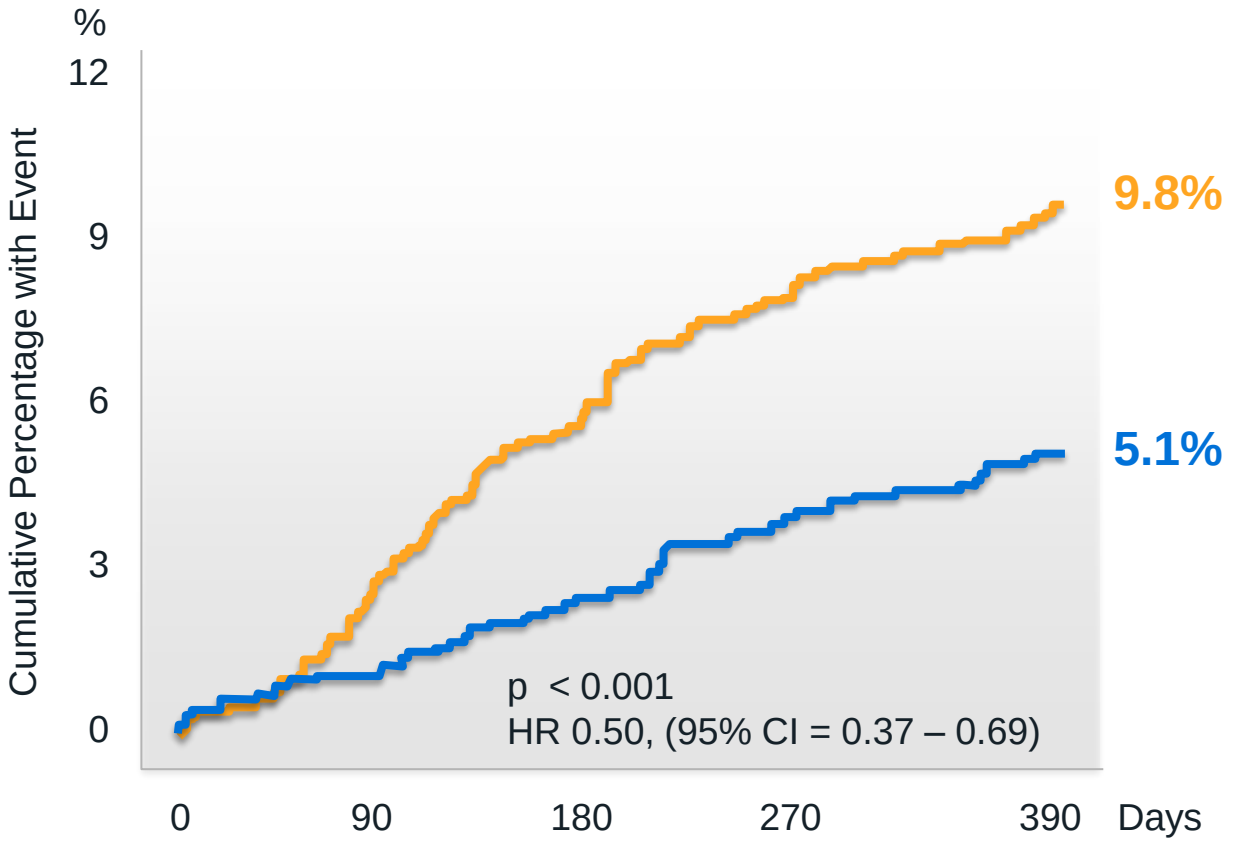
None of the procedure characteristics differ at $p < 0.05$

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)

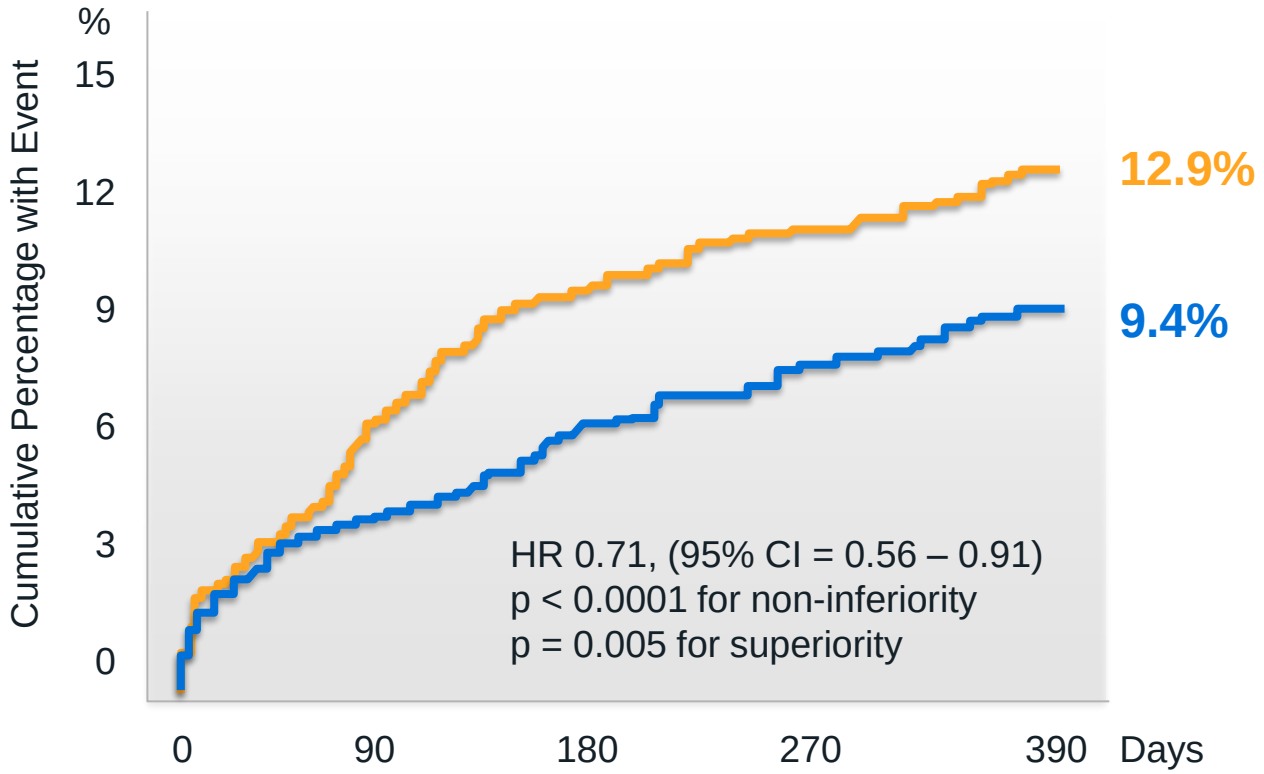


Number at Risk

DCS	1221	1167	1130	1098	1053
BMS	1211	1131	1072	1034	984

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

Primary Safety Endpoint (Cardiac Death, MI, ST)

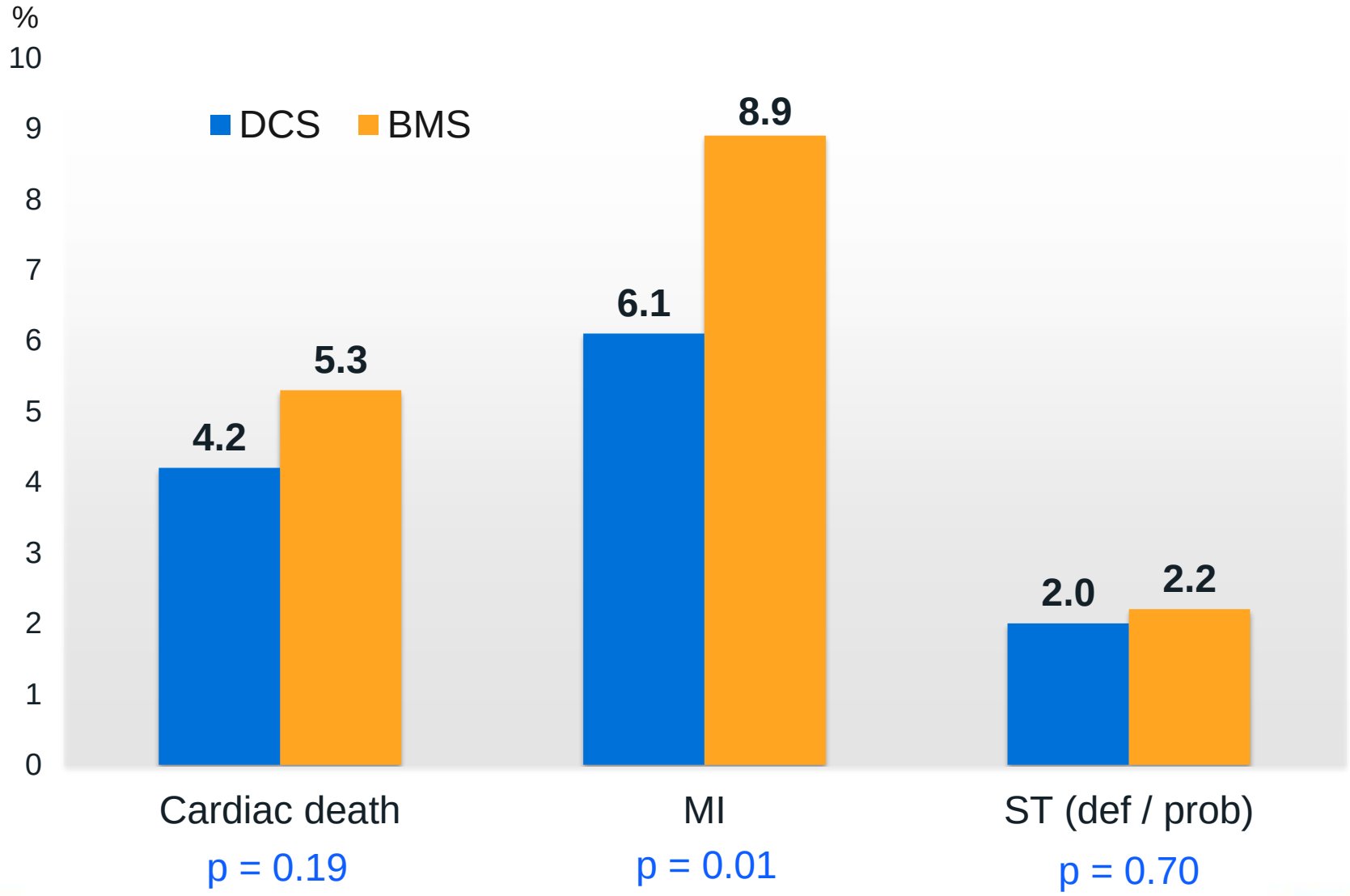


Number at Risk

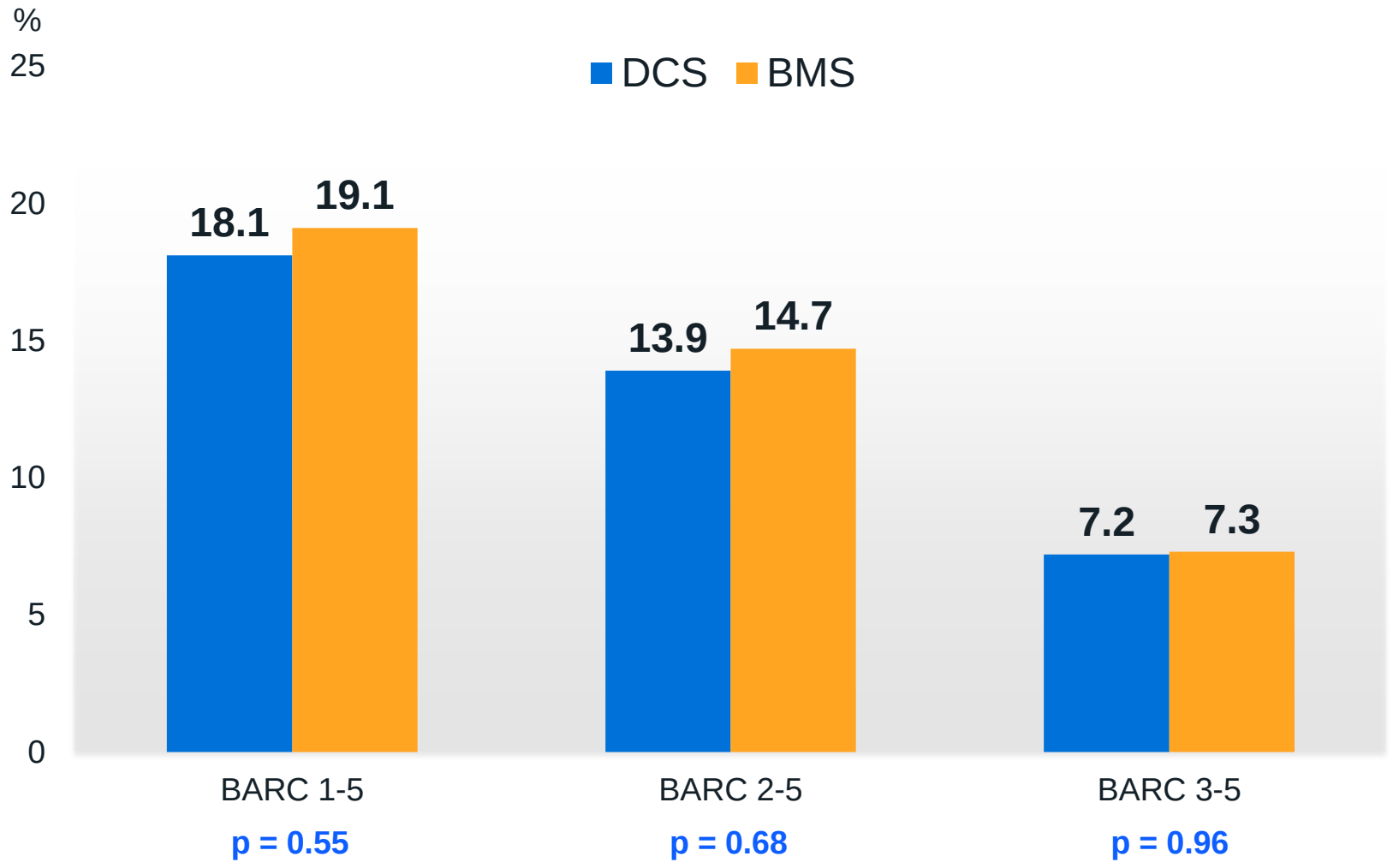
DCS	1221	1146	1105	1081	1045
BMS	1211	1115	1066	1037	1000

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

Components of Safety Endpoint

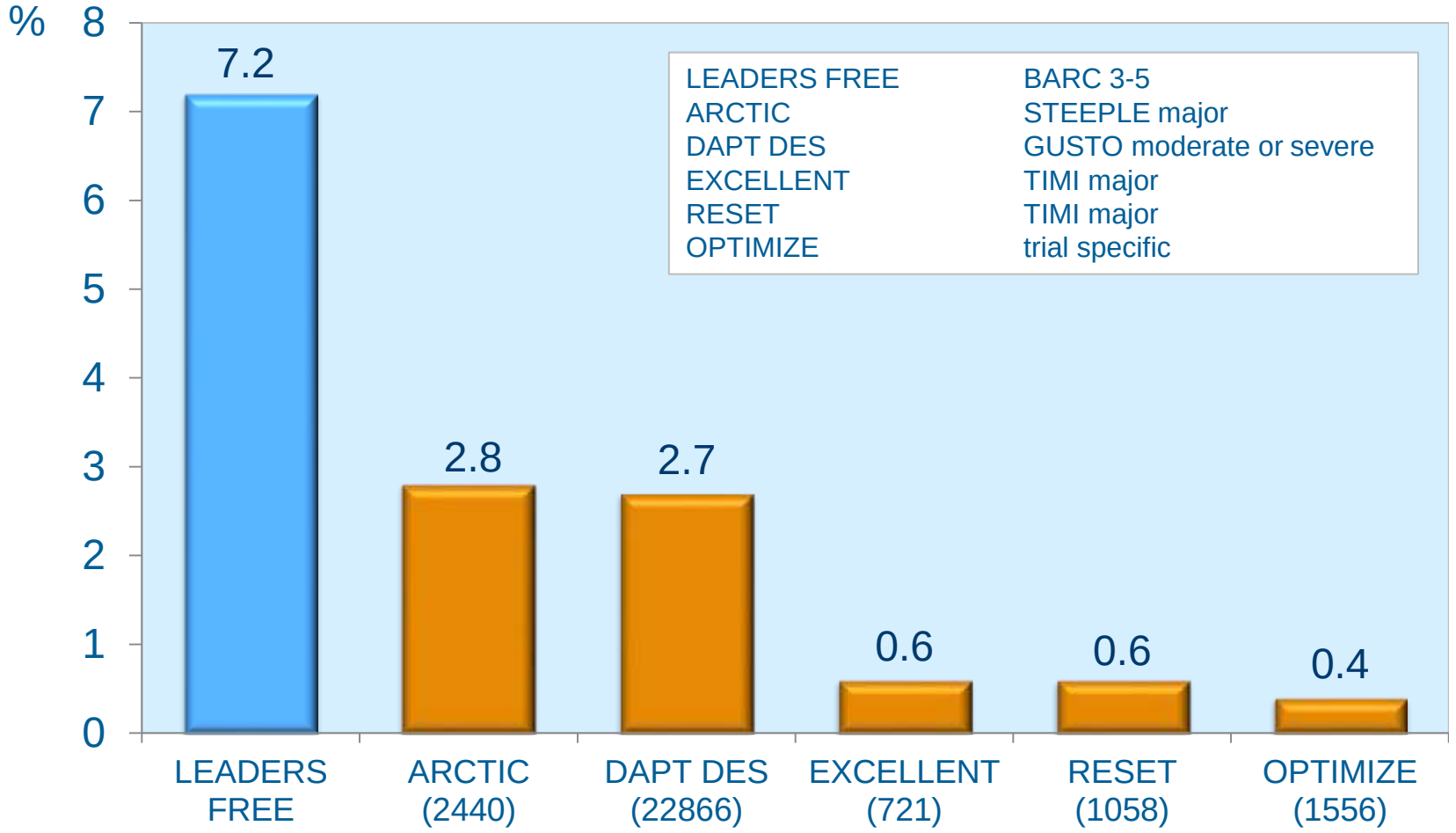


Bleeding During 12 Months Follow-Up



Major bleeding in DES DAPT trials

(first 12 months on DAPT after PCI)

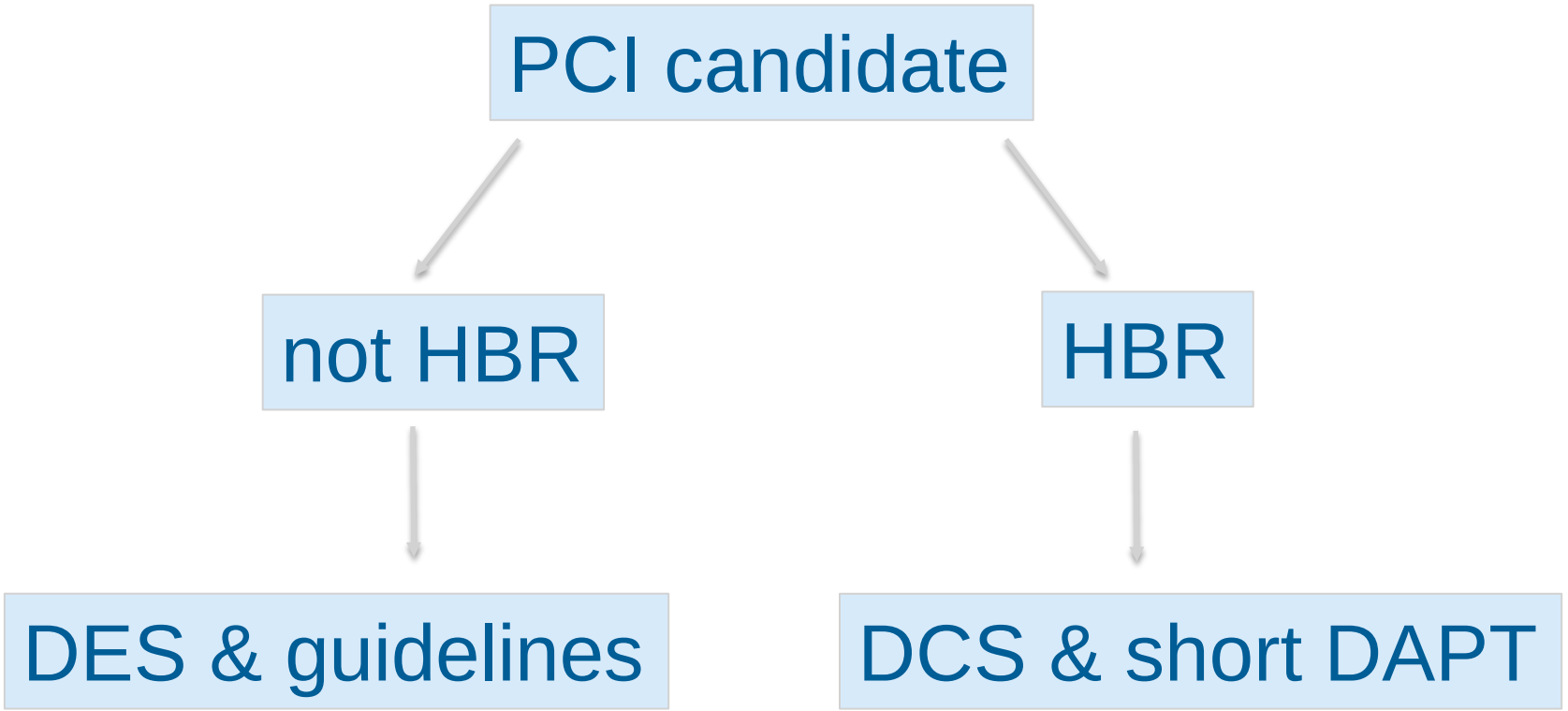


DAPT trials exclusion criteria (✗) vs. LEADERS FREE inclusion criteria (✓)

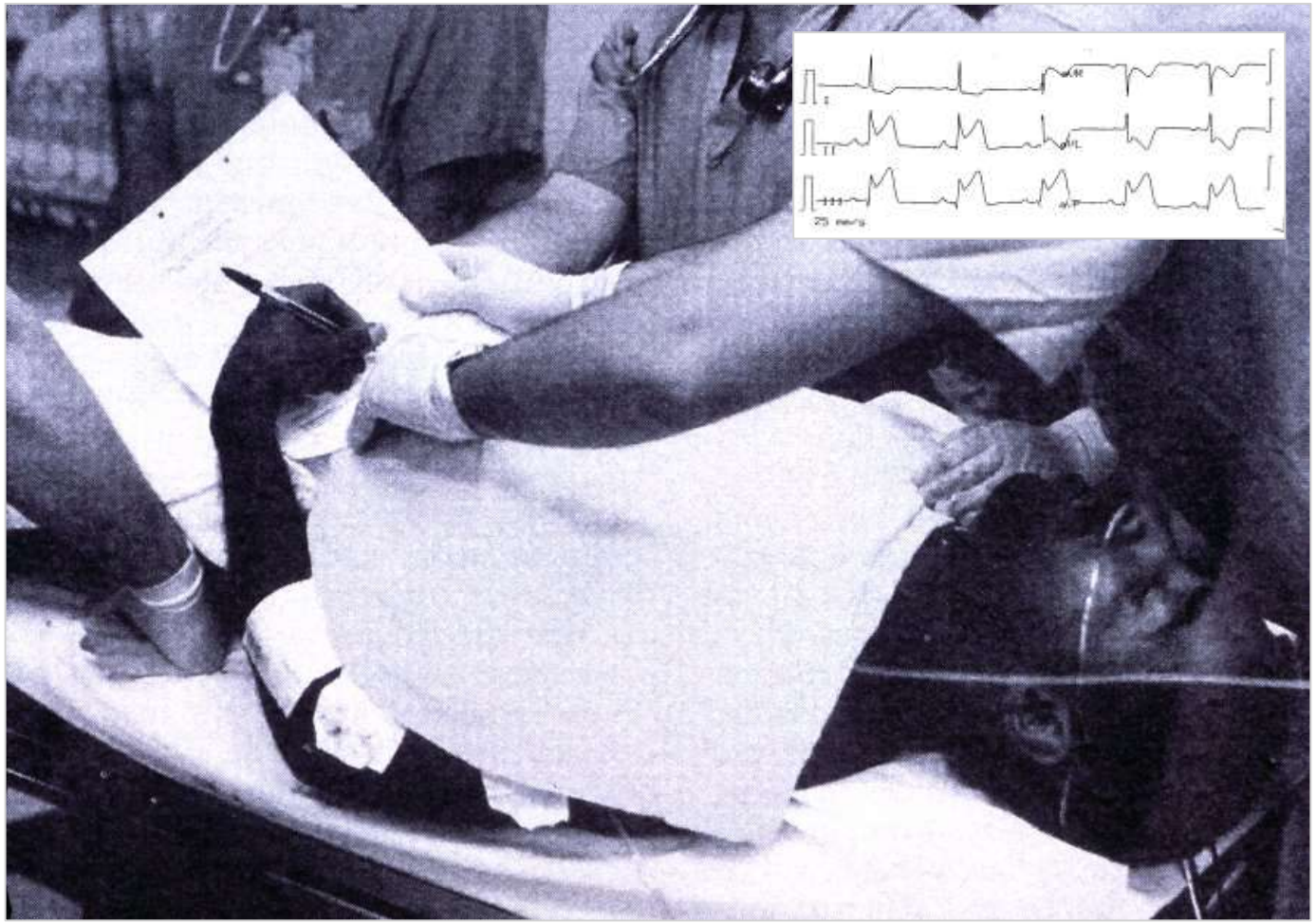
LEADERS FREE

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

There now is a choice…



Detailed medical history?
Lab values?



DES & very short DAPT - two very different questions:

All comers

Is it safe to stop early for selected patients?

RESET (E-ZES 3 mo)
OPTIMIZE (E-ZES 3 mo)

High risk for bleeding

how do DES/DCS compare with a BMS standard, combined with systematic ultra-short DAPT ?

LEADERS FREE (BA9 DCS 1 mo)
ZEUS HBR (E-ZES 32 days)

- 2117 patients
- 1ary EP: CV death, MI, ST, TVR or bleeding

E-ZES + 3 mo DAPT
vs.
SES, EES or R-ZES + 12 mo DAPT

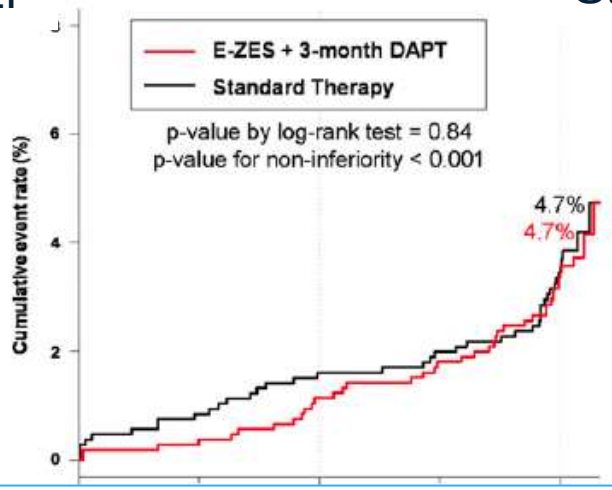
A New Strategy for Discontinuation of Dual Antiplatelet Therapy

The RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation)

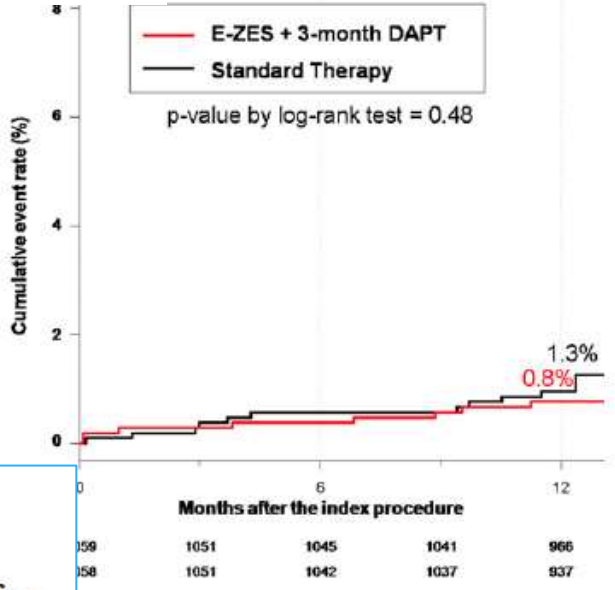
Byeong-Keuk Kim, MD,* Myeong-Ki Hong, MD,*† Dong-Ho Shin, MD, MPH,* Chung-Mo Nam, PhD,‡ Jung-Sun Kim, MD,* Young-Guk Ko, MD,* Donghoon Choi, MD,* Tae-Soo Kang, MD,§ Byoung-Eun Park, MD,§ Woong-Chol Kang, MD,‖ Seung-Hwan Lee, MD,¶ Jung-Han Yoon, MD,¶ Bum-Kee Hong, MD,# Hyuck-Moon Kwon, MD,# Yangsoo Jang, MD,*† for the RESET Investigators

Seoul, Cheonan, Incheon, and Wonju, Republic of Korea

Primary EP



Stent thrombosis



Major bleeding
E-ZES: 0.2%
Control: 0.6%

Conclusions

E-ZES+3-month DAPT could be safe and beneficial for the selected patients with coronary artery disease who may need to stop DAPT early after DES implantation.

JACC 2012; 60: 1340-8

E-ZES vs. a thin-strut BMS + 30 days DAPT

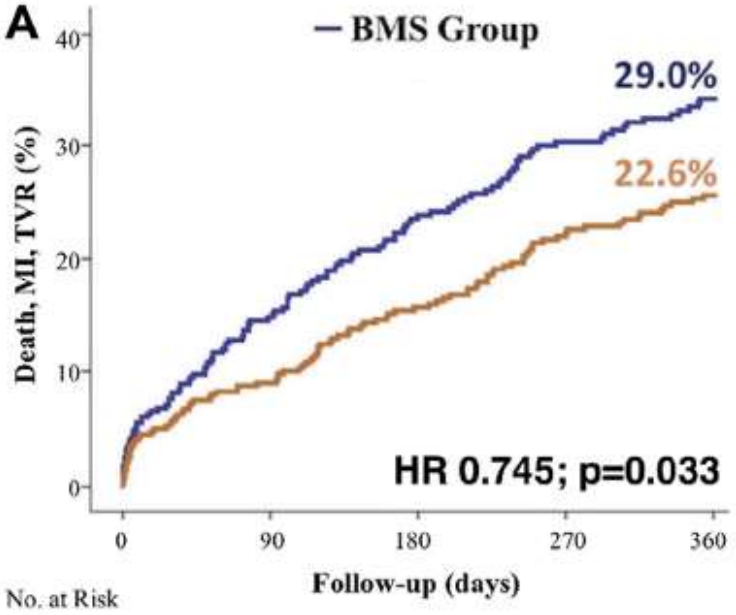
- 828 HBR patients
- 1^{ary} EP: death, MI, TVR

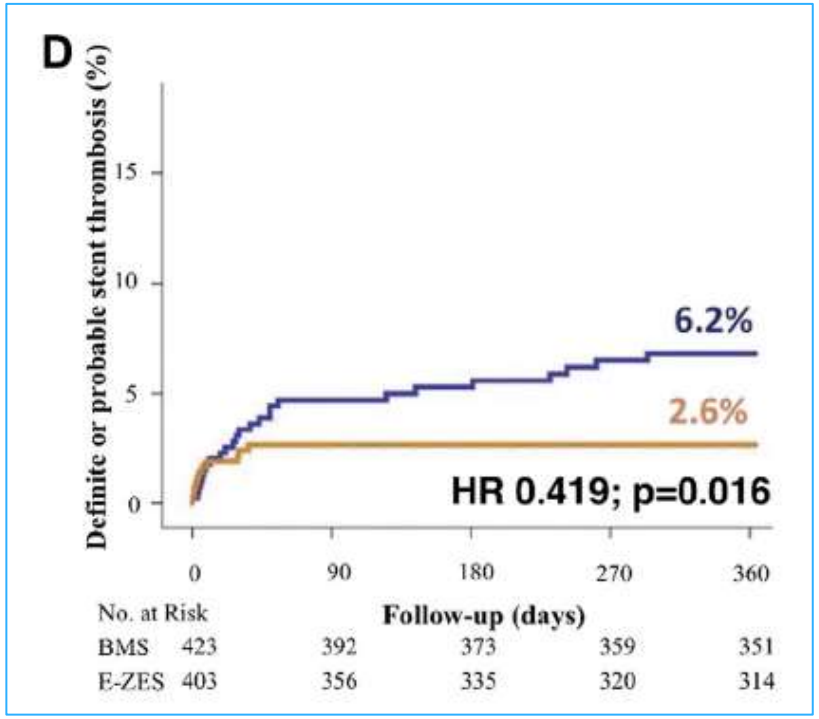
HBR

Is Bare-Metal Stent Implantation Still Justifiable in High Bleeding Risk Patients Undergoing Percutaneous Coronary Intervention?

A Pre-Specified Analysis From the ZEUS Trial

Sara Ariotti, MD,[a,b] Marianna Adamo, MD,[b] Francesco Costa, MD,[b] Athanasios Patialiakas, MD,[c] Carlo Briguori, MD, PhD,[d] Attila Thury, MD, PhD,[e] Salvatore Colangelo, MD,[f] Gianluca Campo, MD,[g] Matteo Tebaldi, MD,[g] Imre Ungi, MD, PhD,[e] Stefano Tondi, MD,[h] Marco Roffi, MD,[i] Alberto Menozzi, MD, PhD,[i] Nicoletta de Cesare, MD,[k] Roberto Garbo, MD,[f] Emanuele Meliga, MD,[l] Luca Testa, MD, PhD,[m] Henrique Mesquita Gabriel, MD,[n] Marco Ferlini, MD,[o] Pascal Vranckx, MD, PhD,[p] Marco Valgimigli, MD, PhD,[a,b] for the ZEUS Investigators





CONCLUSIONS

Our study provides proof of concept that in HBR patients who undergo stent implantation, E-ZES as compared with conventional BMS followed by 30-day DAPT regimen provides superior efficacy and safety.

JACC intv 2016; 9: 426-36

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)

- ✓ Patients with undetermined/doubtful bleeding risk and/or DAPT compliance may constitute a logical group of further candidates for a DCS
- ✓ Use of BMS can only be justified today for economic reasons
- ✓ The BioFreedom DCS with 1 month DAPT should be considered as the current default therapy for HBR patients

Late-breaking data at Euro PCR 2016

- LEADERS-FREE ACS

  Christoph Naber

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

  Philip Urban

Thank you