

# High Bleeding Risk Patients With DES: Insights from SENIOR and LEADER-FREE Trials

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TCTAP 2018 Seoul

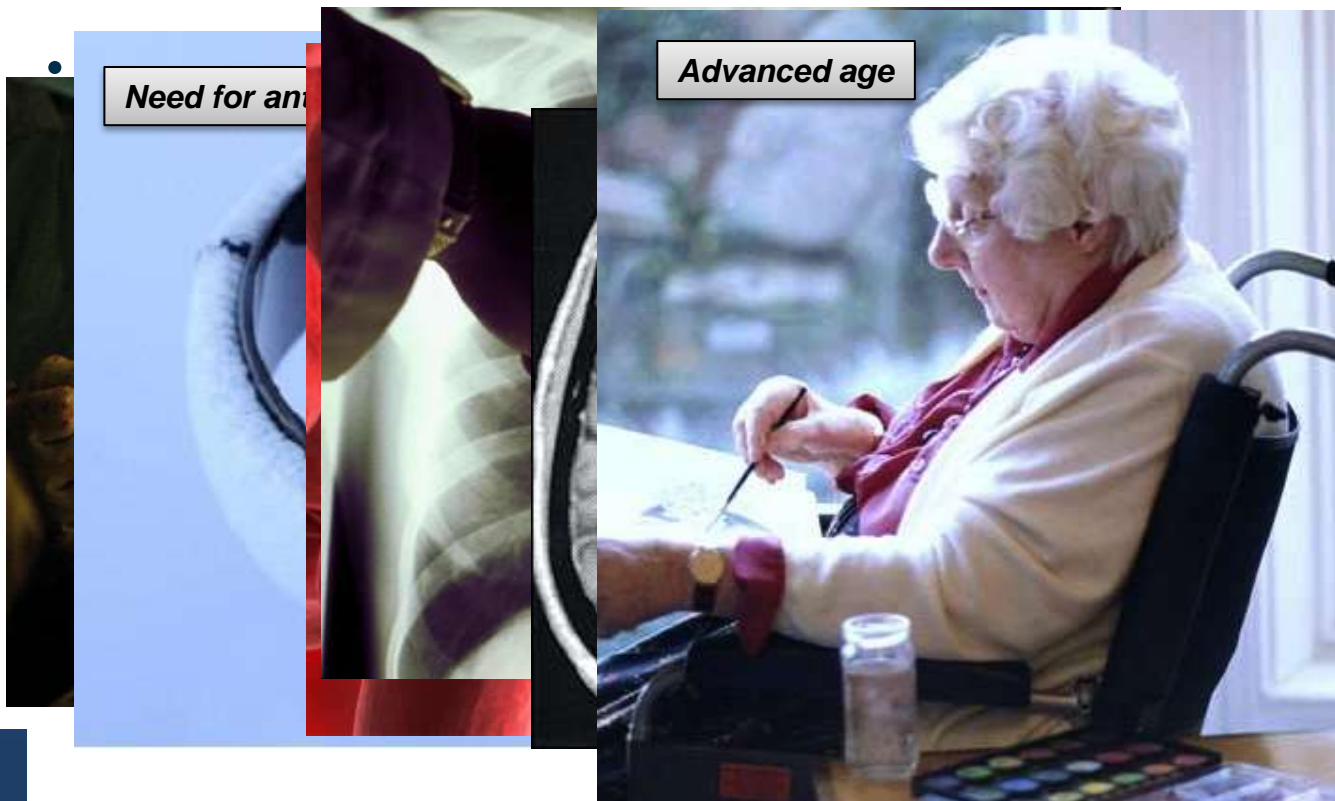
# Disclosure Statement of Financial Interest

I, Marie Claude Morice am shareholder and CEO of CERC, the CRO conducting the Leaders free and Master DAPT trials

# The High bleeding risk patient

- Who are they?

# High Bleeding Risk Patients (HBR)

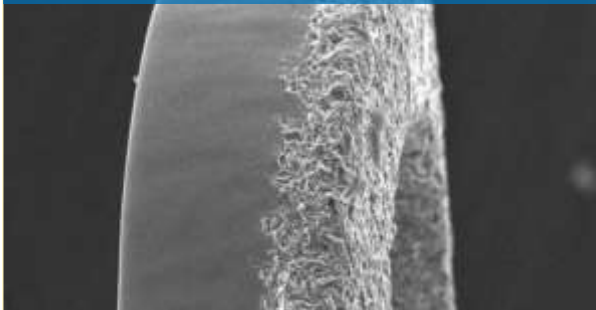


# DAPT « all comers » trials exclusion criteria ( X ) vs. LEADERS FREE inclusion criteria ( ✓ )

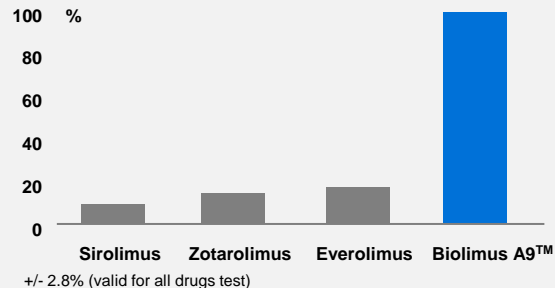
	EXCELLENT	RESET	ARCTIC	OPTIMIZE	DAPT DES	LEADERS FREE
Low Hb or thrombocytopenia	X	X	X			✓
Recent bleeding	X	X	X			✓
Anticoagulants	X		X		X	✓
Need for surgery	X		X	X	X	✓
Renal or hepatic failure	X	X	X			✓
STEMI and/or GP 2b3a blockers	X		X	X		not excluded
Anticipated difficulties with long term DAPT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

# 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>



## Advantages:

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

# LEADERS FREE Trial Design

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

BioFreedom™  
DCS

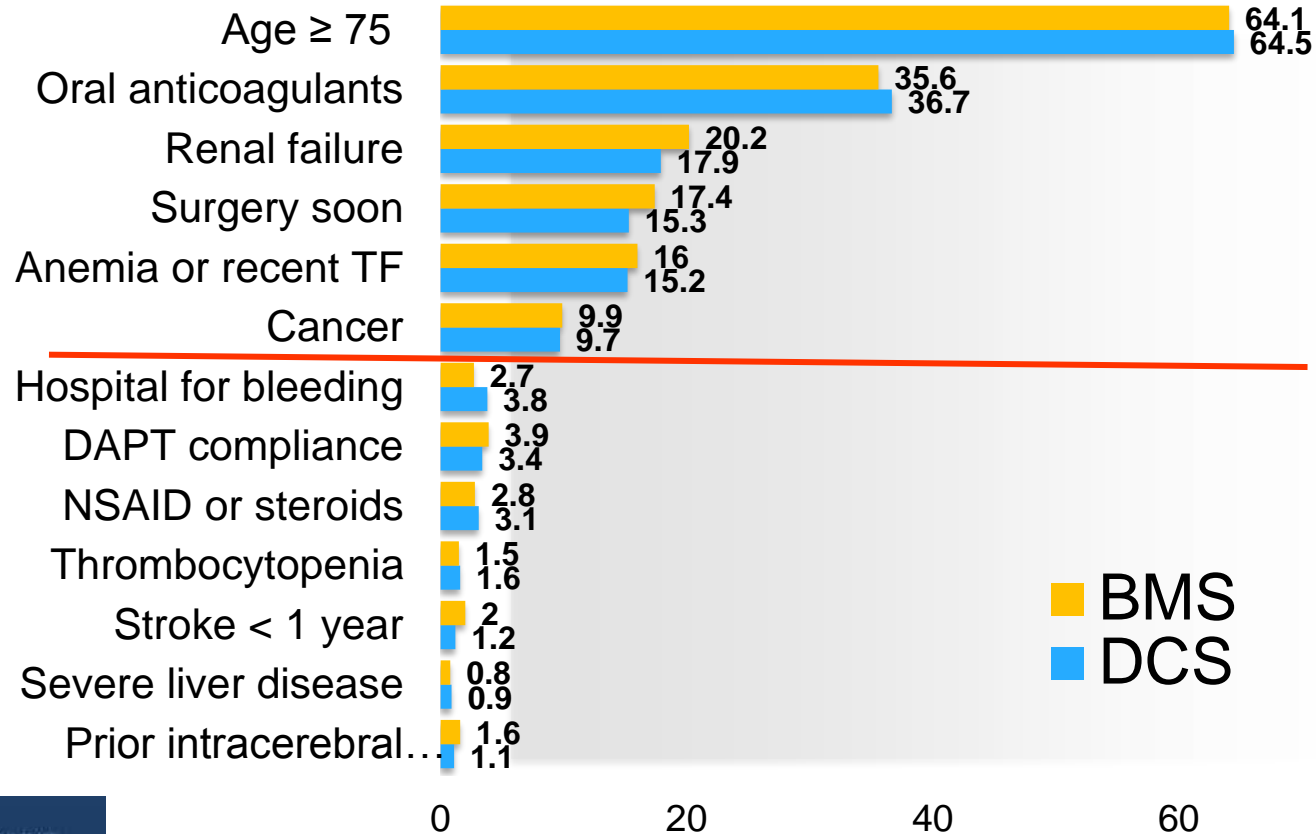
vs.

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)

# Leaders Free Inclusion Criteria Applied (1.7 criteria / patient)

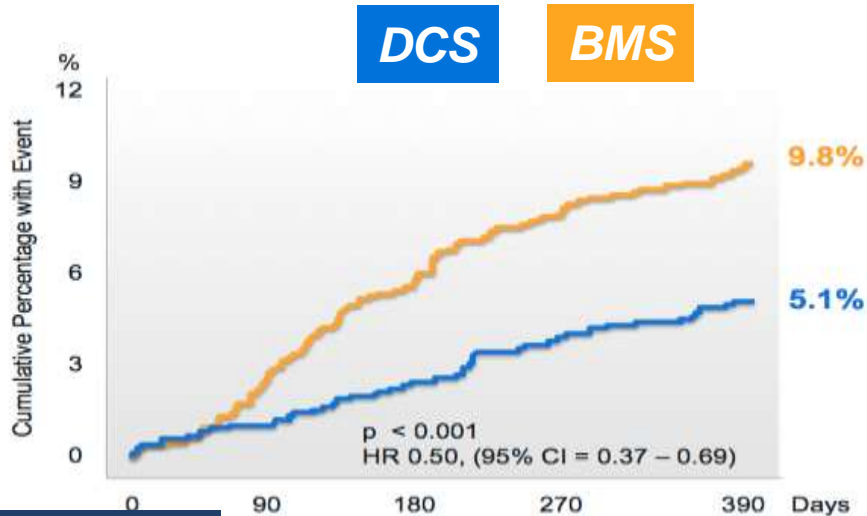


■ BMS  
■ DCS

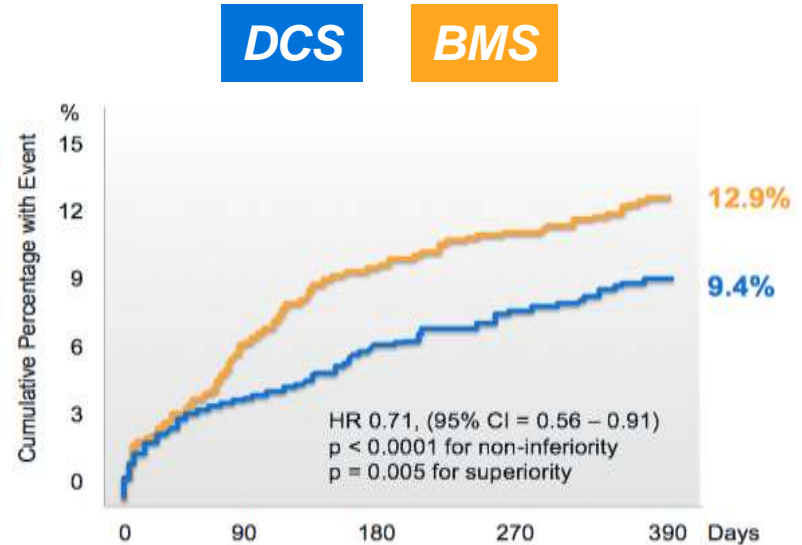


# Leaders free Efficacy and Safety Endpoints @ 1 Years

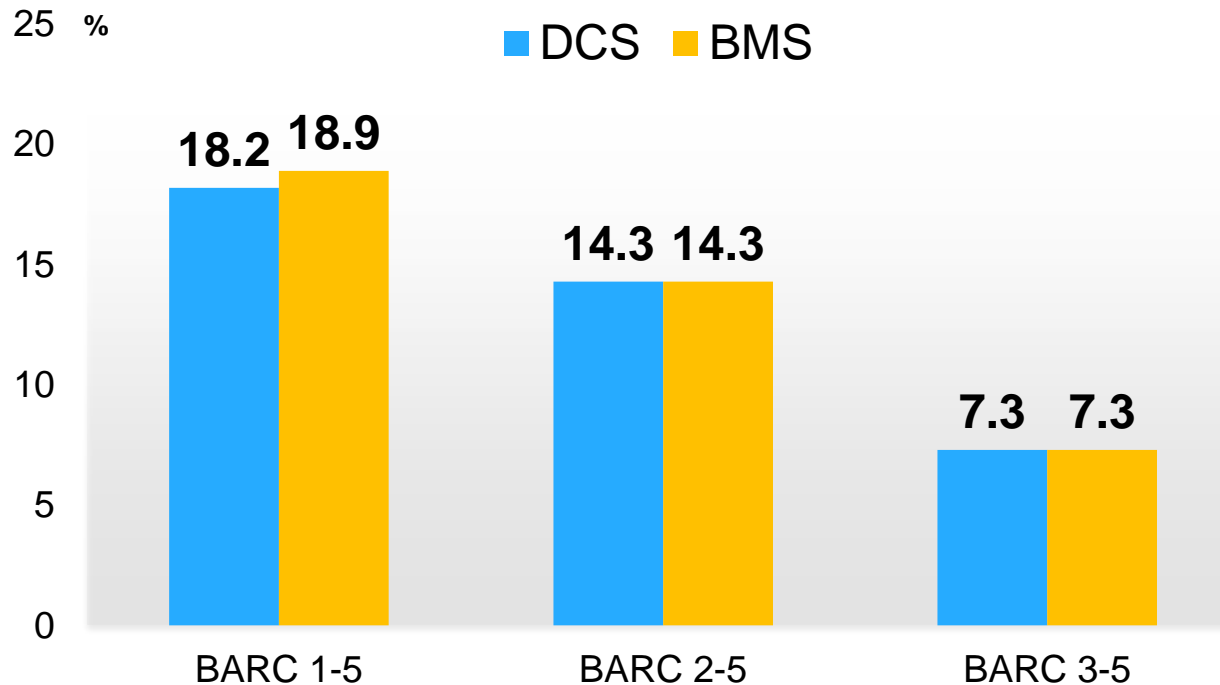
*Efficacy (cd-TLR)*



*Safety (cardiac death, MI, ST)*



# LF Elderly population: Bleeding events



*None of bleeding category differs at  $p < 0.05$*

# SENIOR

## A Randomized Trial of a Bioabsorbable Polymer-Based Metallic DES vs. a BMS with Short DAPT in Patients with Coronary Artery Disease Older than 75 Years.

### The SENIOR Trial

O. Varenne, S. Cook, G. Sideris, S. Kedev, T. Cuisset, D. Carrié, T. Hovasse, P. Garot, R. El Mahmoud, C. Spaulding, G. Helft, J. Diaz Fernandez, S. Brugaletta, E. Pinar Bermudez, J. Mauri Ferre, P. Commeau, E. Teiger, K. Bogearts, M. Sabate, M-C. Morice and P. Sinnaeve,  
for the SENIOR investigators.

# SENIOR Trial design

*Randomized (1:1), single blind trial  
1,200 patients aged 75 years and above*

*Tailored DAPT: 1 mo in stable and 6 mo in ACS pts  
Prespecified by the investigator prior to randomization*

**DES**

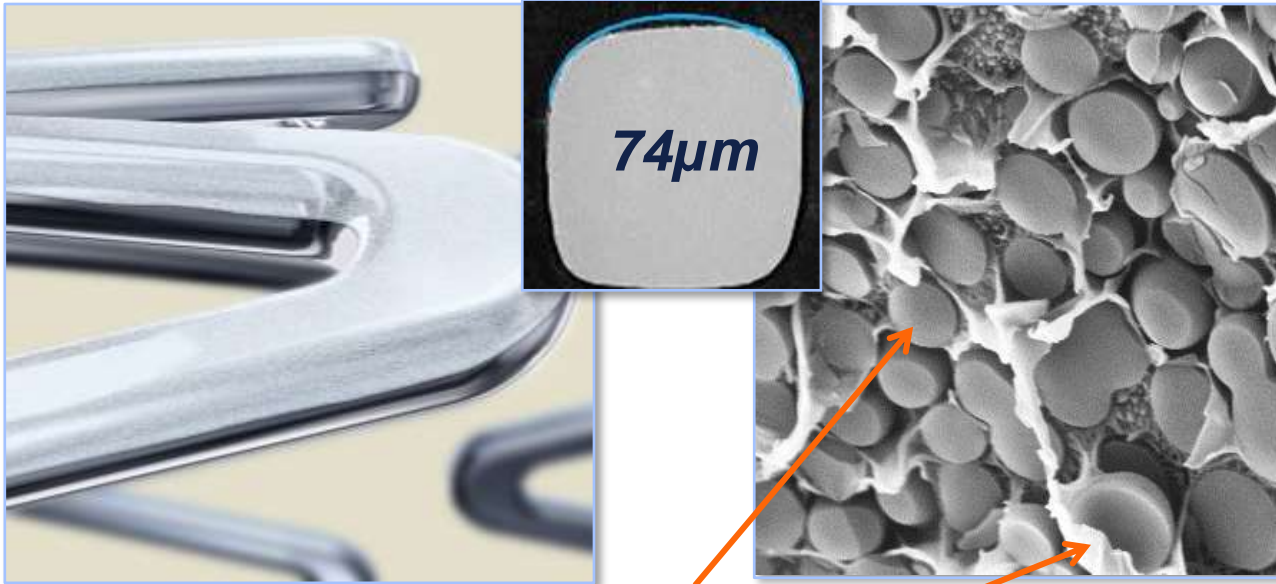
**Vs.**

**BMS**

**Primary End Point 1y: all-cause mortality, non-fatal MI, stroke,  
IDTLR**

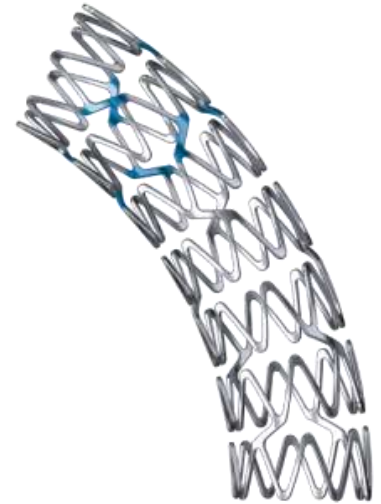
**Secondary End Points 1y: Bleeding BARC 2-5/3-5, stent  
thrombosis**

# Synergy™ DES used in SENIOR



**Everolimus  
PLGA  
Polymer**

**SEM of coating  
(x5000)**



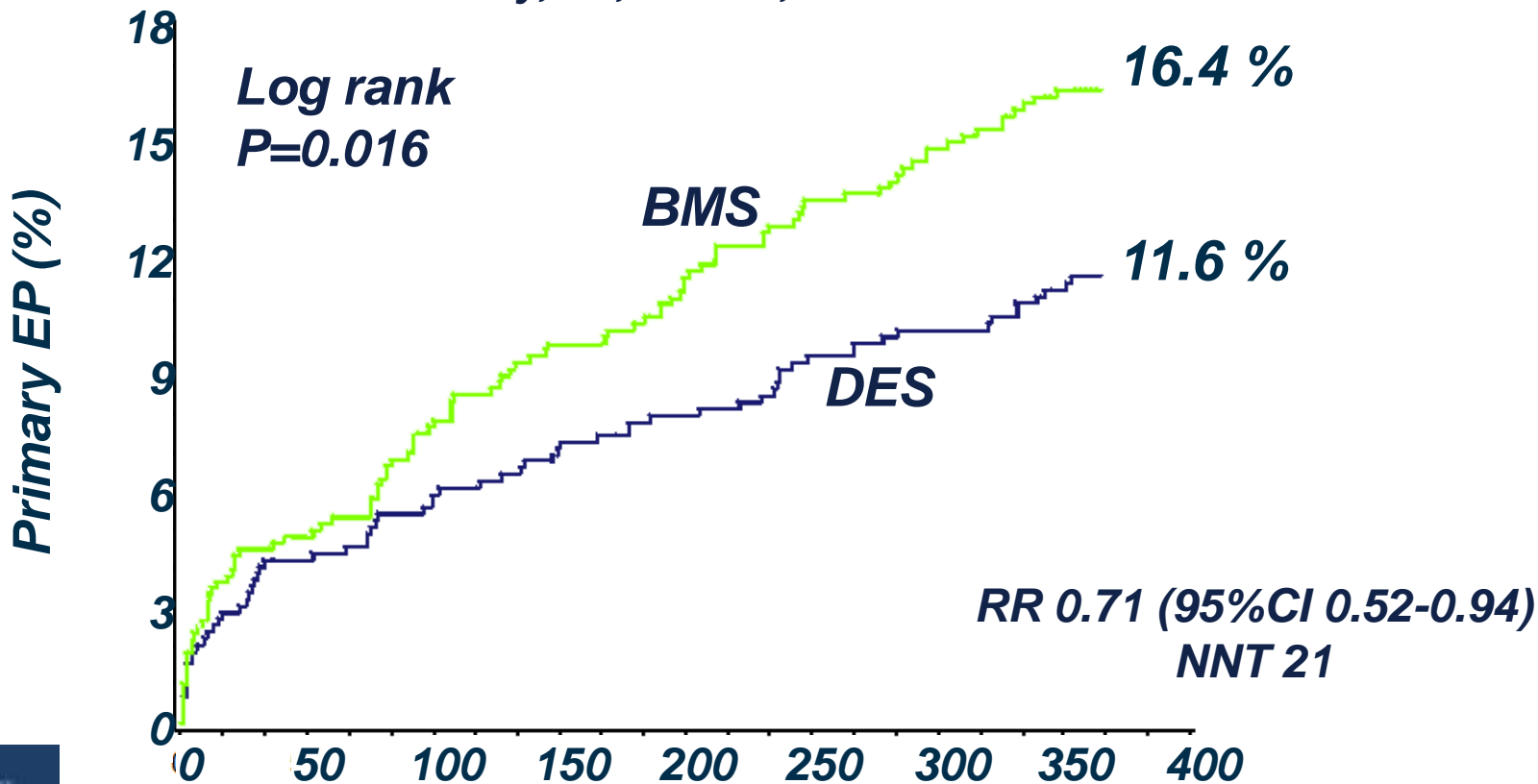
**BMS**

**SENIOR**

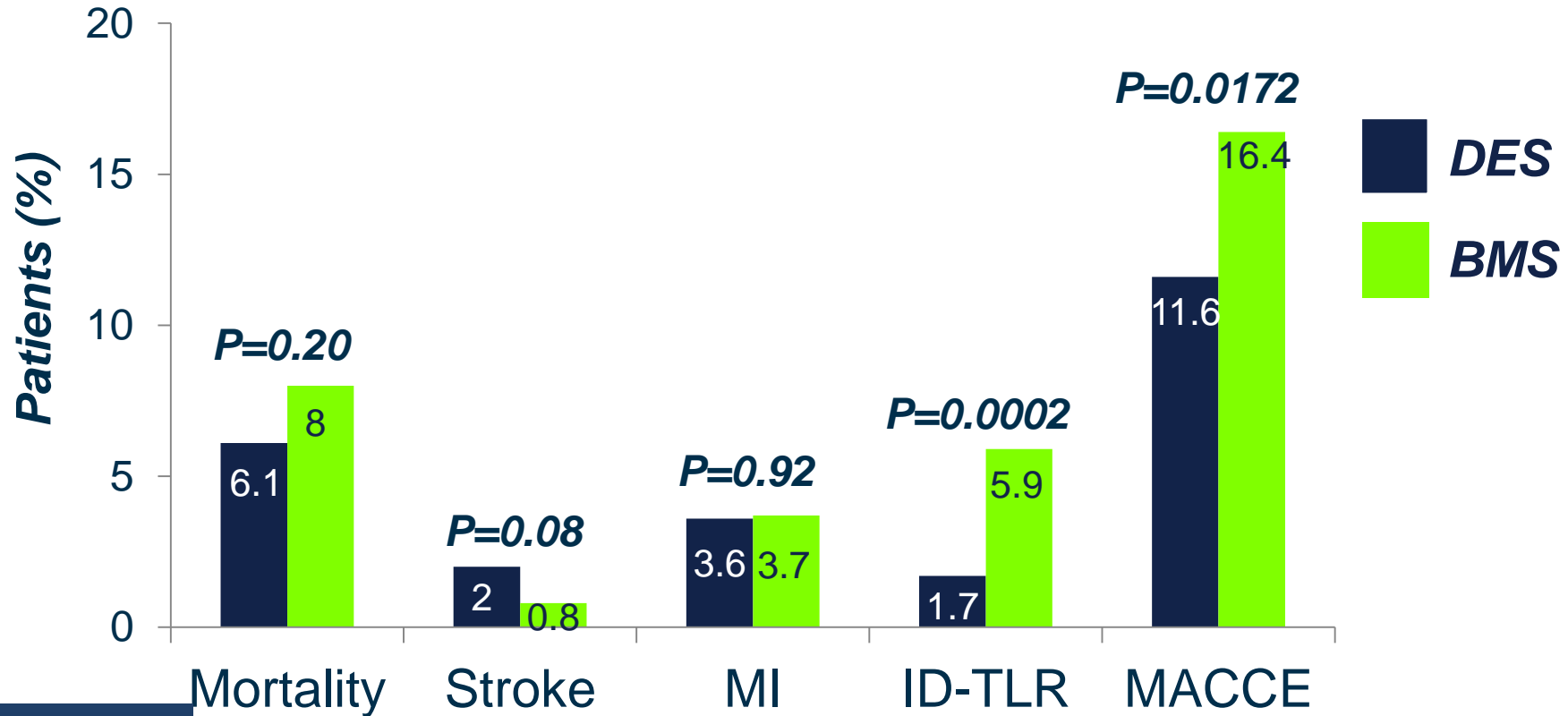
*Meredith I. et al. EuroInterv 2017 (in Press) doi:10.4244/EU-D-17-00529*

# Primary End Point

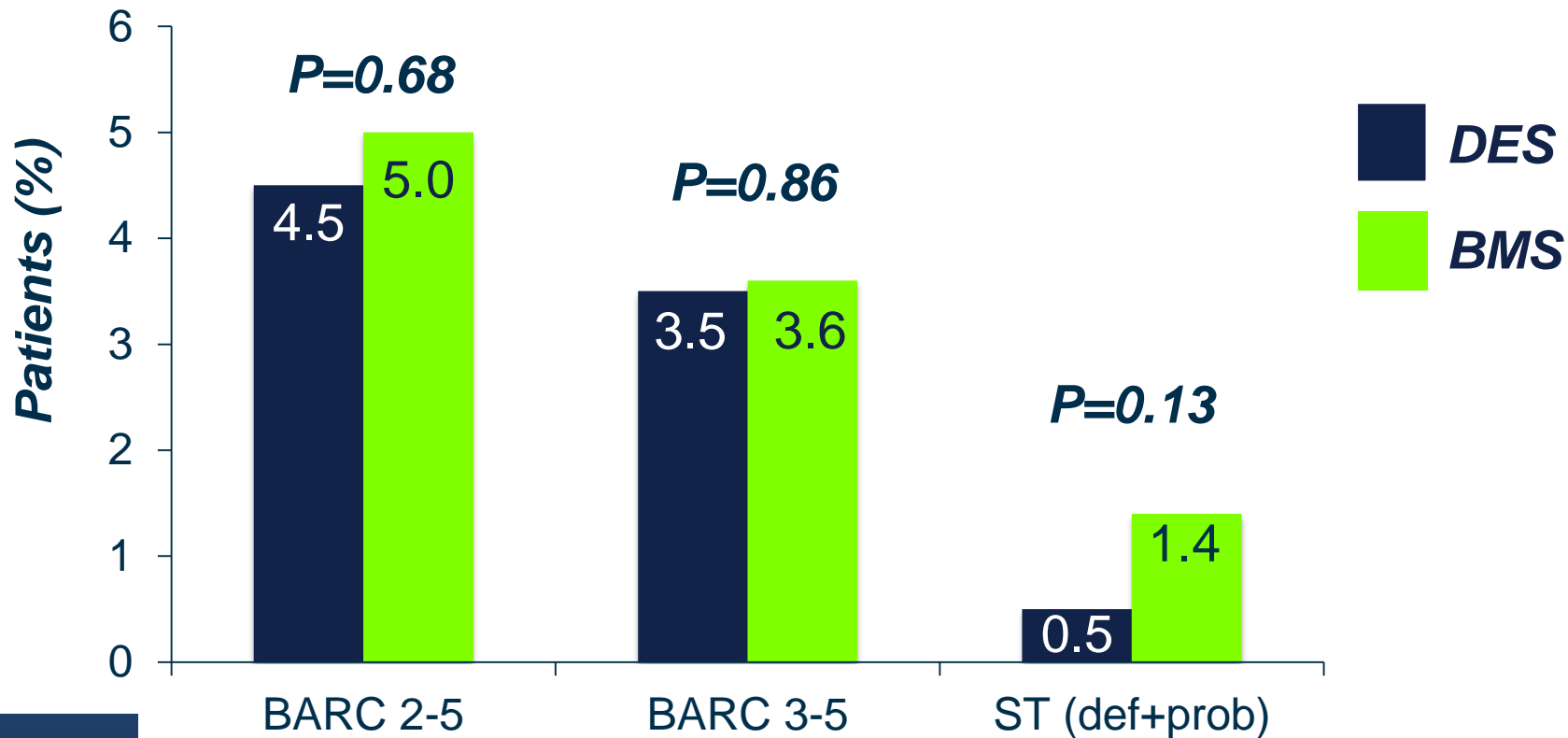
All-cause mortality, MI, stroke, ischemia-driven TLR



# MACCE Components



# Safety Endpoints

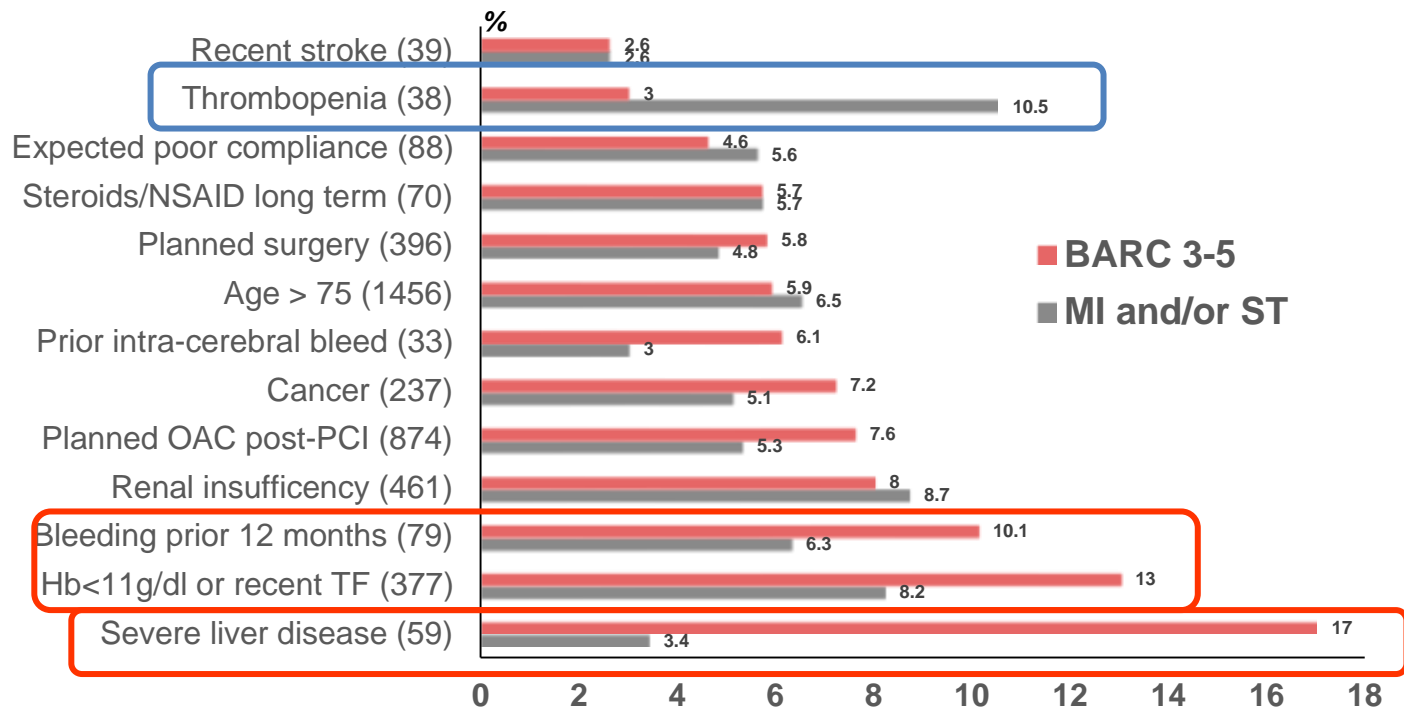




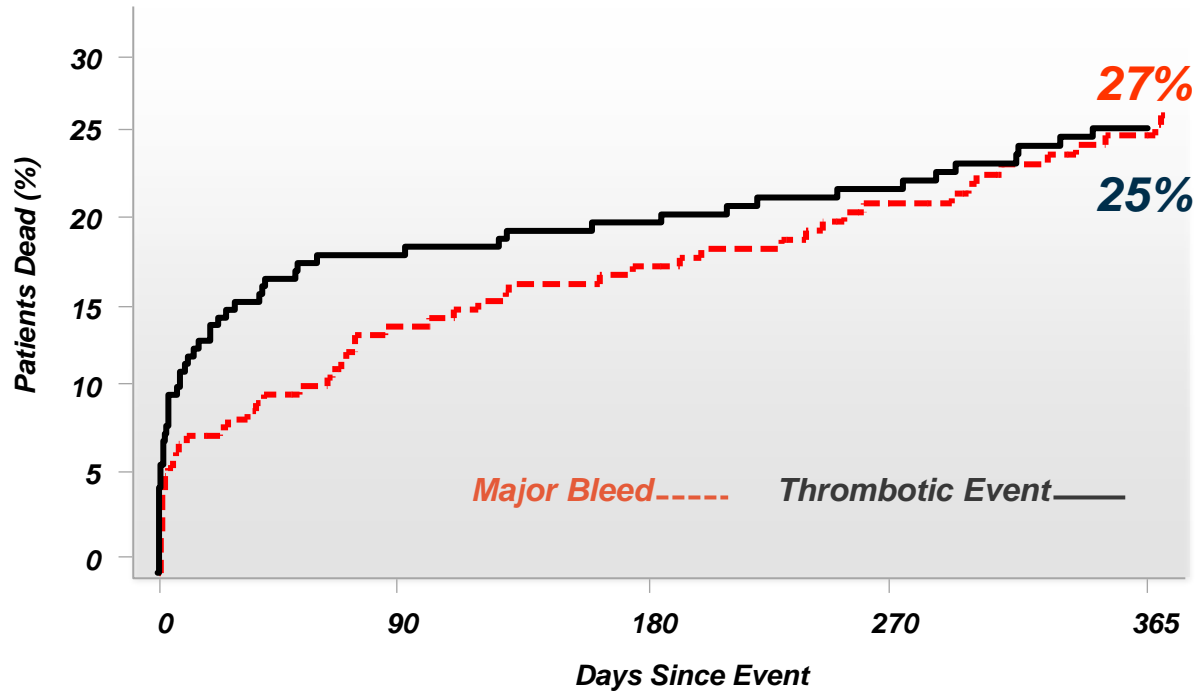
# The High bleeding risk patient

- **Some criteria of HBR are also predicting thrombotic events.....**

# First coronary thrombotic or major bleeding events according to LEADERS FREE inclusion criteria\*



# Leaders Free: 1-year Mortality Following Major Bleed (BARC 3-5) or Coronary Thrombotic Event (MI and/or ST)



*Mortality was 6% after 1 year for patients without thrombotic or major bleeding events*

# The High bleeding risk patient

- Does the scores helps?

# 2017 ESC Focused Update on DAPT in Coronary Artery Disease

(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

**Table 3** Risk scores validated for dual antiplatelet therapy duration decision-making

	PRECISE-DAPT score <sup>18</sup>	DAPT score <sup>15</sup>
Time of use	At the time of coronary stenting	After 12 months of uneventful DAPT
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)
Score calculation <sup>a</sup>	<p>HB <math>\geq 12</math> 11.5 11 10.5 &lt;10</p> <p>WBC <math>\leq 5</math> 8 10 12 14 16 18 <math>\geq 20</math></p> <p>Age <math>\leq 50</math> 60 70 80 <math>\geq 90</math></p> <p>CrCl <math>\geq 100</math> 80 60 40 20 0</p> <p>Prior Bleeding No Yes</p> <p>Score Points 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30</p>	<p>Age <math>\geq 75</math> -2 pt 65 to &lt;75 -1 pt &lt;65 0 pt</p> <p>Cigarette smoking +1 pt</p> <p>Diabetes mellitus +1 pt</p> <p>MI at presentation +1 pt</p> <p>Prior PCI or prior MI +1 pt</p> <p>Paclitaxel-eluting stent +1 pt</p> <p>Stent diameter &lt;3 mm +1 pt</p> <p>CHF or LVEF &lt;30% +2 pt</p> <p>Vein graft stent +2 pt</p>
Score range	0 to 100 points	-2 to 10 points
Decision making cut-off suggested	Score $\geq 25$ → Short DAPT Score <25 → Standard/long DAPT	Score $\geq 2$ → Long DAPT Score <2 → Standard DAPT
Calculator	<a href="http://www.precisedaptscore.com">www.precisedaptscore.com</a>	<a href="http://www.daptstudy.org">www.daptstudy.org</a>

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# Coronary Thrombosis and Major Bleeding After PCI With Drug-Eluting Stents

J Am Coll Cardiol 2016;67:2224–34

## Risk Scores From PARIS

Usman Baber, MD, MS,<sup>a</sup> Roxana Mehran, MD,<sup>a</sup> Gennaro Giustino, MD,<sup>a</sup> David J. Cohen, MD, MSc,<sup>b</sup>

**TABLE 4 Integer Risk Score for Major Bleeding**

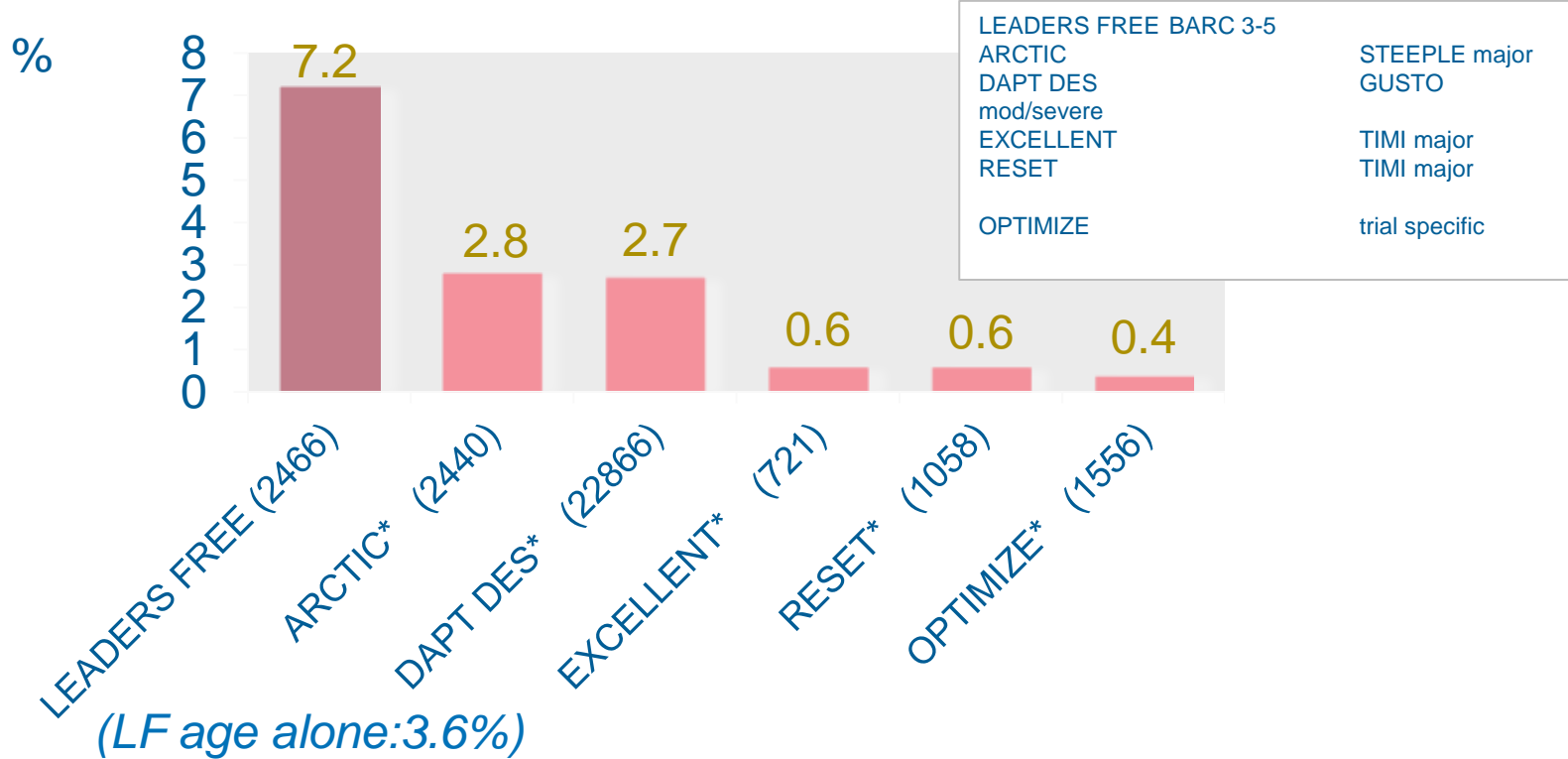
Parameter	Score
Age, yrs	
<50	0
50–59	–1
60–69	–2
70–79	+3
≥80	+4
BMI, kg/m <sup>2</sup>	
<25	+2
25–34.9	0
≥35	–2
Current smoking	
Yes	+2
No	0
Anemia	
Present	–3
Absent	0
CrCl <60 mL/min	
Present	+2
Absent	0
Triple therapy on discharge	
Yes	+2
No	0

**TABLE 5 Integer Risk Score for Coronary Thrombotic Events**

Parameter	Score
Diabetes mellitus	
None	0
Non-insulin-dependent	+1
Insulin-dependent	+3
Acute coronary syndrome	
No	0
Yes, Tn-negative	+1
Yes, Tn-positive	+2
Current smoking	
Yes	+1
No	0
CrCl <60 mL/min	
Present	+2
Absent	0
Prior PCI	
Yes	+2
No	0
Prior CABG	
Yes	+2
No	0

Tn = troponin; other abbreviations as in Table 1.

# Major bleeding during first year



# The HBR patients, unanswered questions

- \* Which age limit to qualify for HBR?*
- \* For patients on oral anticoagulant, - how long should DAPT be?*
- \* renal failure alone?*
- \* Cancer ( about 10% in LF) which disease to treat first?*
- \* Should we use risk scores? If yes which one? (no dedicated HBR score, for example, DAPT score can be applied after one year of DAPT only.....)*
- \* Wich DAPT optimal duration for HBR?*



***MAnagement of high bleeding risk patients post bioresorbable polymer coated STEnt implantation with an abbReviated versus prolonged DAPT regimen – MASTER DAPT***

***Ultimaster, 4300pts, 110 sites, 60 countries, near 1000 pts randomised***



# ***The ARC HBR initiative***

***Leads Philip Urban, Marie Claude Morice, Roxana Mehran, Mitch Krucoff***

## ***List of experts:***

*Robert Byrne, Roisin Colleran, Davide Capodanno, Thomas Cuisset, Pedro Eedermans, John Gregson, Michael Haude, Stephan James, Marco Valgimigli, Dominic Angiolillo, Don Cuplic, John Eikelboom, Matthew Price, Sunil Rao, Roseann White, Hyo soo Kim, Takeshi Kimura, Michael Gibson, Norman Stockbridge, John Lashinger, Darren Mylotte, Olivier Varenne, Andrew Farb, Gerrit Anne Van Es, Robert Yeh.*

***First meeting in Washington done in April***

# IN SUMMARY remaining gaps:

## Identification of HBR patients

*Scores vs clinical judgment, dedicated score needed  
Age and OAC are main factors, but many others exists, (major / minor criteria) role of the ARC HBR task force*

## PCI strategies specific to HBR patients

*Dedicated devices? , no room for BMS, are all last generation DES disconnected from DAPT duration? Optimal PCI technic*

## Antithrombotic strategies tailored for HBR patients

*Awaiting DAPT duration trials results ( Master DAPT)*