

**Patients à Haut risque de saignement,
balance du risque thrombotique/ risque
hémorragique,
leçons de Leaders free et Senior**

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Massy France**

APPAC, Biarritz, Juin 2018

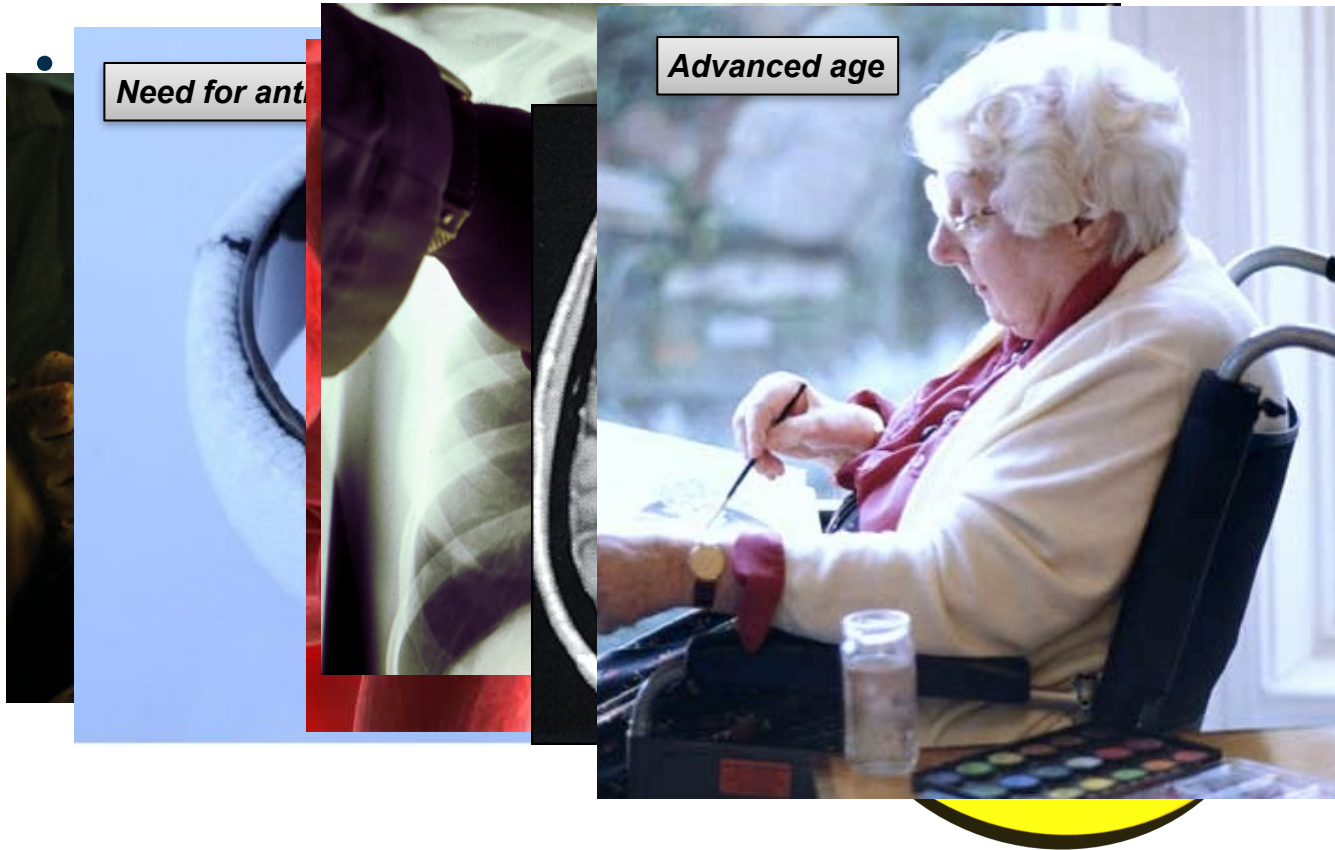
Disclosure Statement of Financial Interest

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

Les patients à haut risque de saignement

- Qui sont ils?

Patients à haut risque hémorragique (HBR)

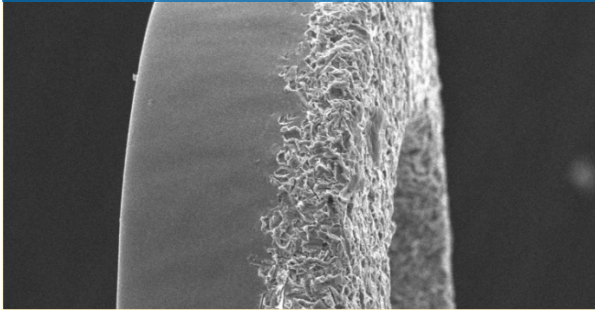


DAPT « all comers » critères d'exclusion(X) vs. LEADERS FREE critère d'inclusion(✓)

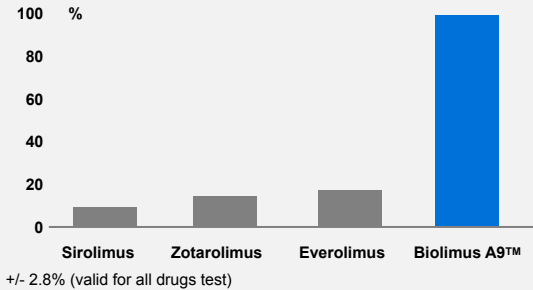
	EXCELLENT	RESET	ARCTIC	OPTIMIZE	DAPT DES	LEADERS FREE
Low Hb or thrombocytopenia	X	X	X			✓
Recent bleeding	X	X	X			✓
Anticoagulants	X		X		X	✓
Need for surgery	X		X	X	X	✓
Renal or hepatic failure	X	X	X			✓
STEMI and/or GP 2b3a blockers	X		X	X		not excluded
Anticipated difficulties with long term DAPT	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 Sirolimus¹



Advantages:

- Avoid any possible polymer-related adverse effects
- Rapid drug transfer to vessel wall (98% within one month²)
- 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

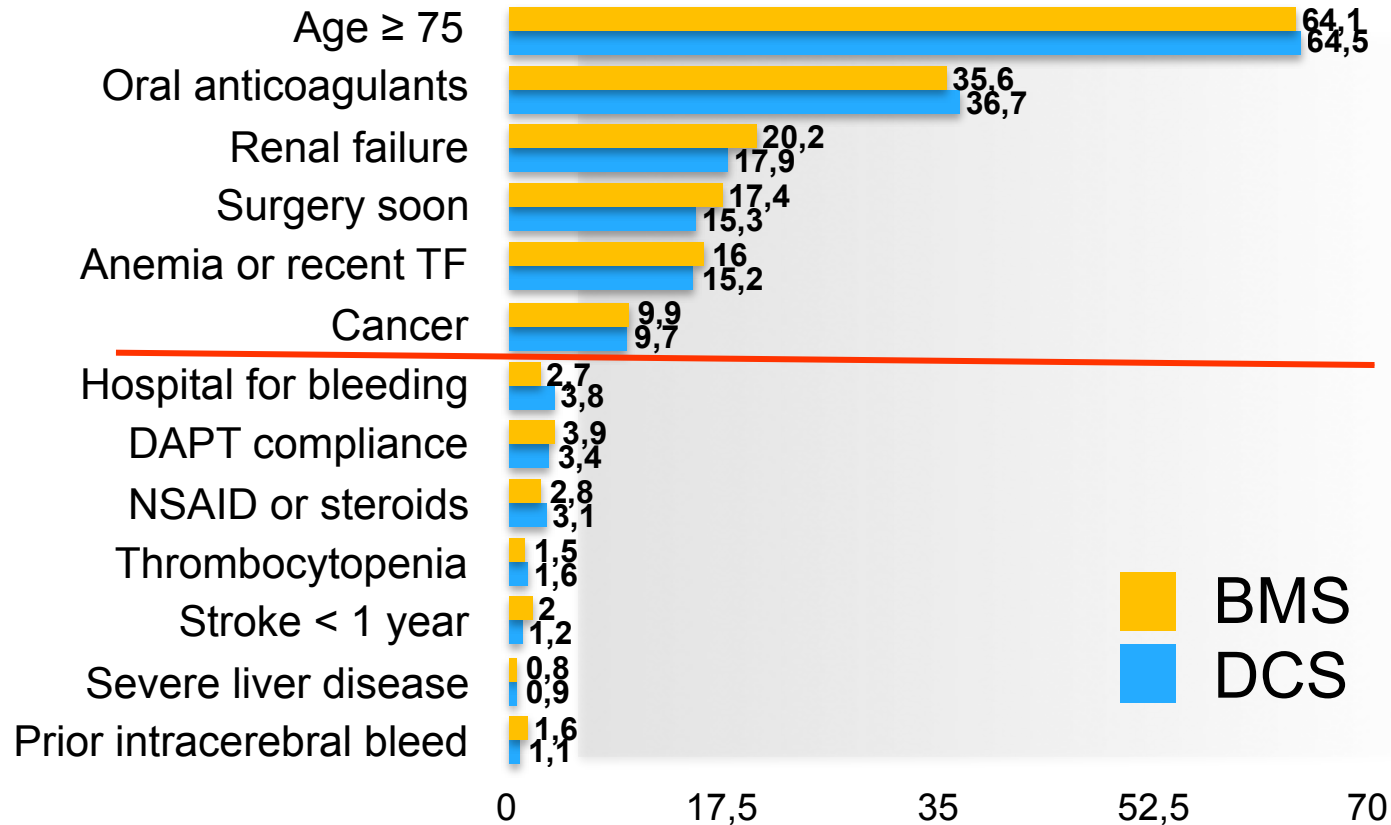
vs.

Gazelle™
BMS

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

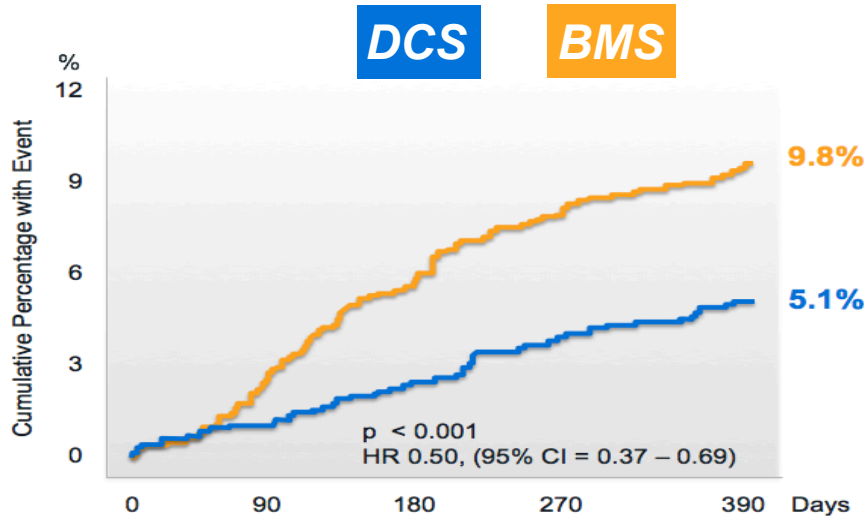
- **Primary safety endpoint:**
Composite of cardiac death, MI, definite / probable stent thrombosis
at 1 year (non-inferiority then superiority)
- **Primary efficacy endpoint:**
Clinically-driven TLR at 1 year (superiority)

Leaders Free Inclusion Criteria Applied (1.7 criteria / patient)

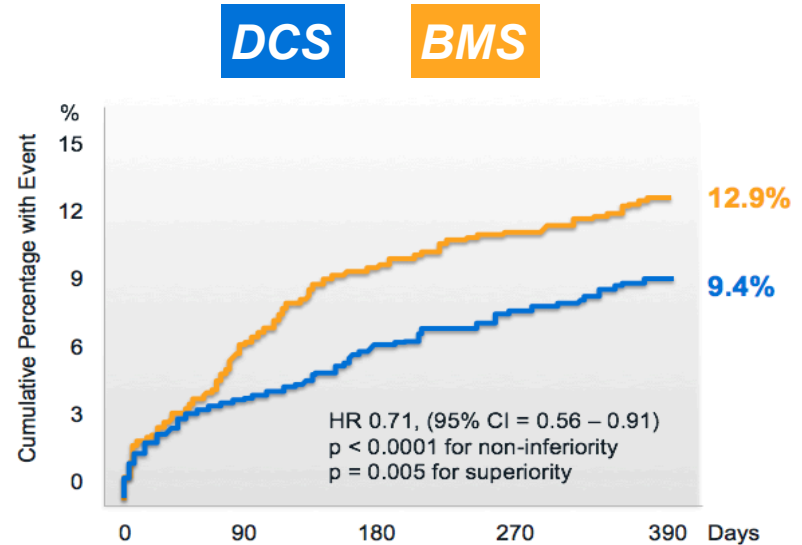


Leaders free Efficacy and Safety Endpoints @ 1 Years

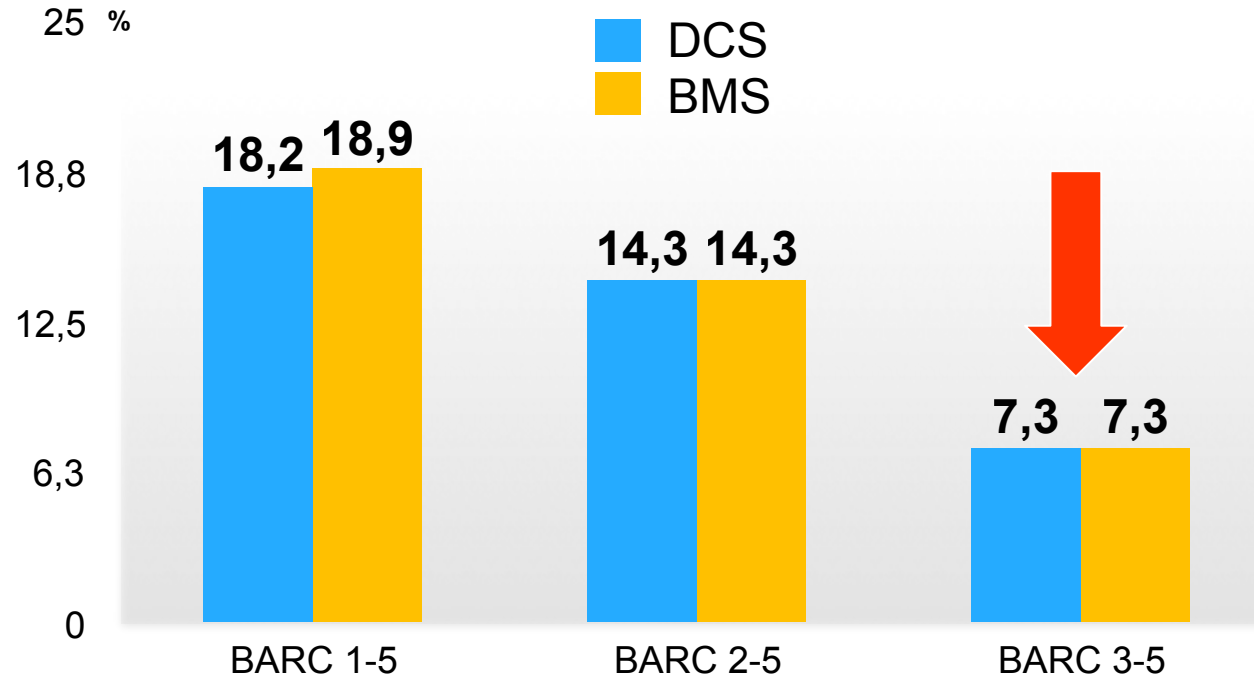
Efficacy (cd-TLR)



Safety (cardiac death, MI, ST)



LF Elderly population: Bleeding events



None of bleeding category differs at $p < 0.05$

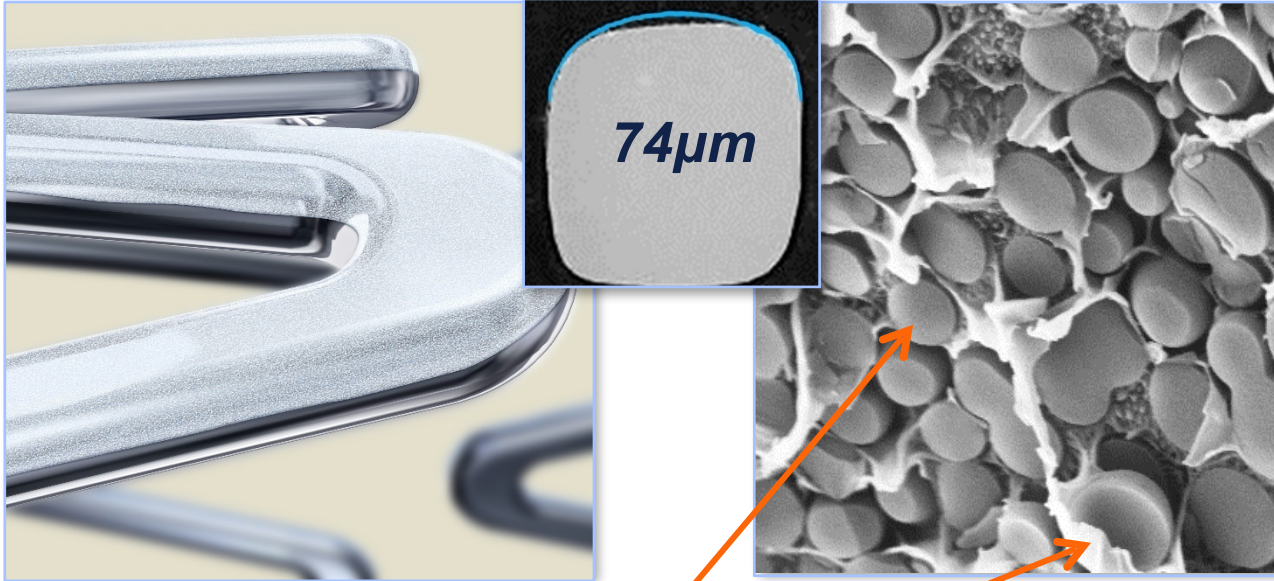
SENIOR

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

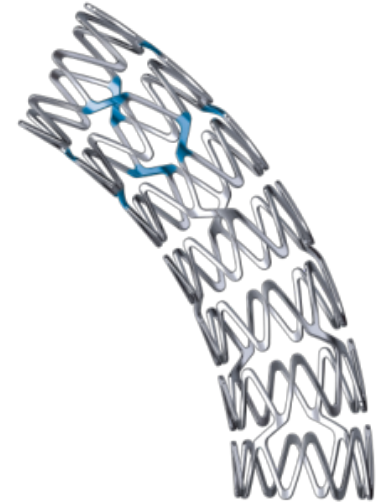
O. Varenne, S. Cook, G. Sideris, S. Kedev, T. Cuisset, D. Carrié, T. Hovasse, P. Garot, R. El Mahmoud, C. Spaulding, G. Helft, J. Diaz Fernandez, S. Brugaletta, E. Pinar Bermudez, J. Mauri Ferre, P. Commeau, E. Teiger,
K. Bogearts, M. Sabate, M-C. Morice and P. Sinnaeve,
for the SENIOR investigators.

Synergy™ DES used in SENIOR



**Everolimus
PLGA Polymer**

**SEM of coating
(x5000)**



BMS

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

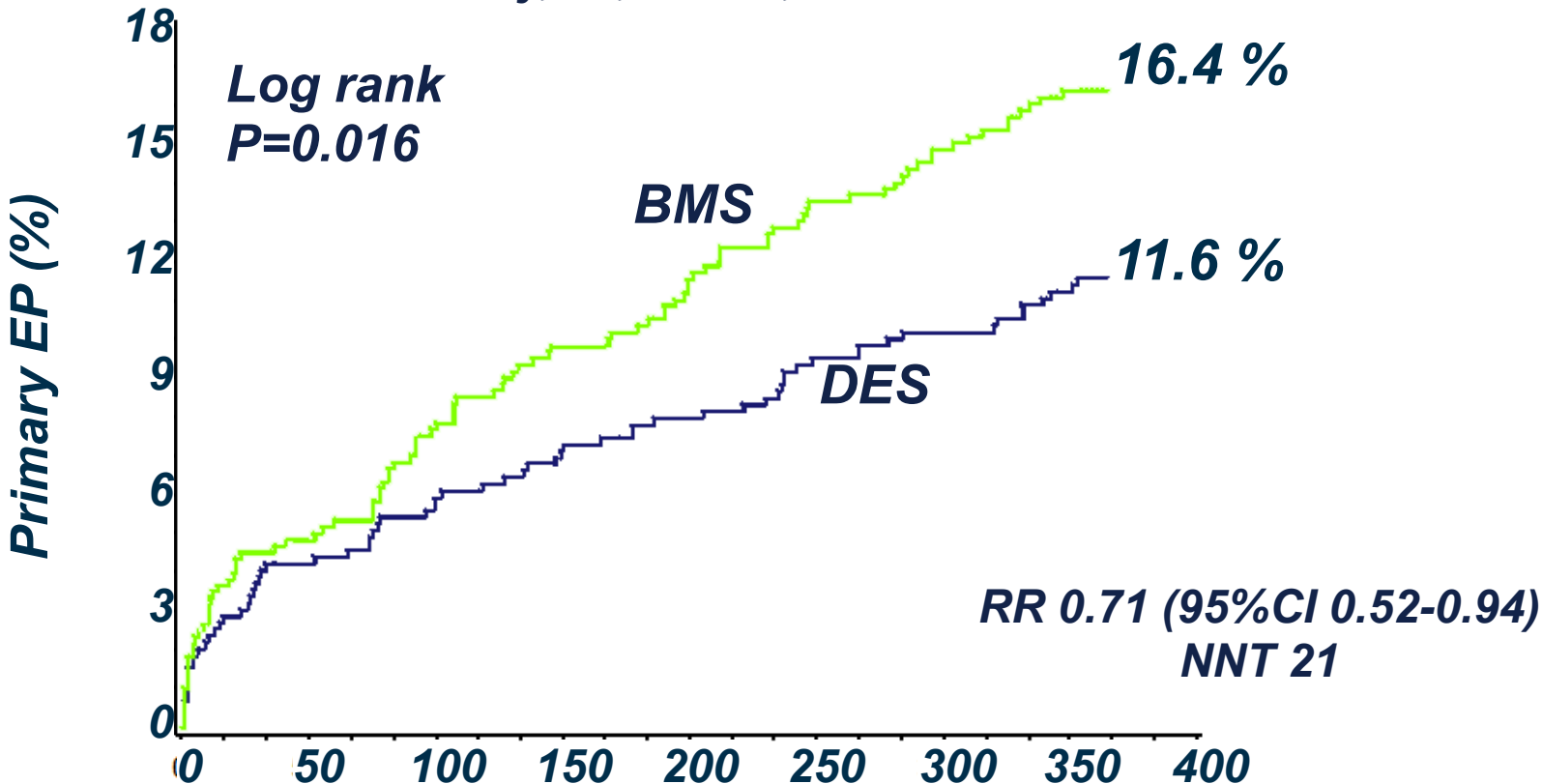
*Primary End Point 1y: all-cause mortality, non-fatal MI, stroke,
IDTLR*

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

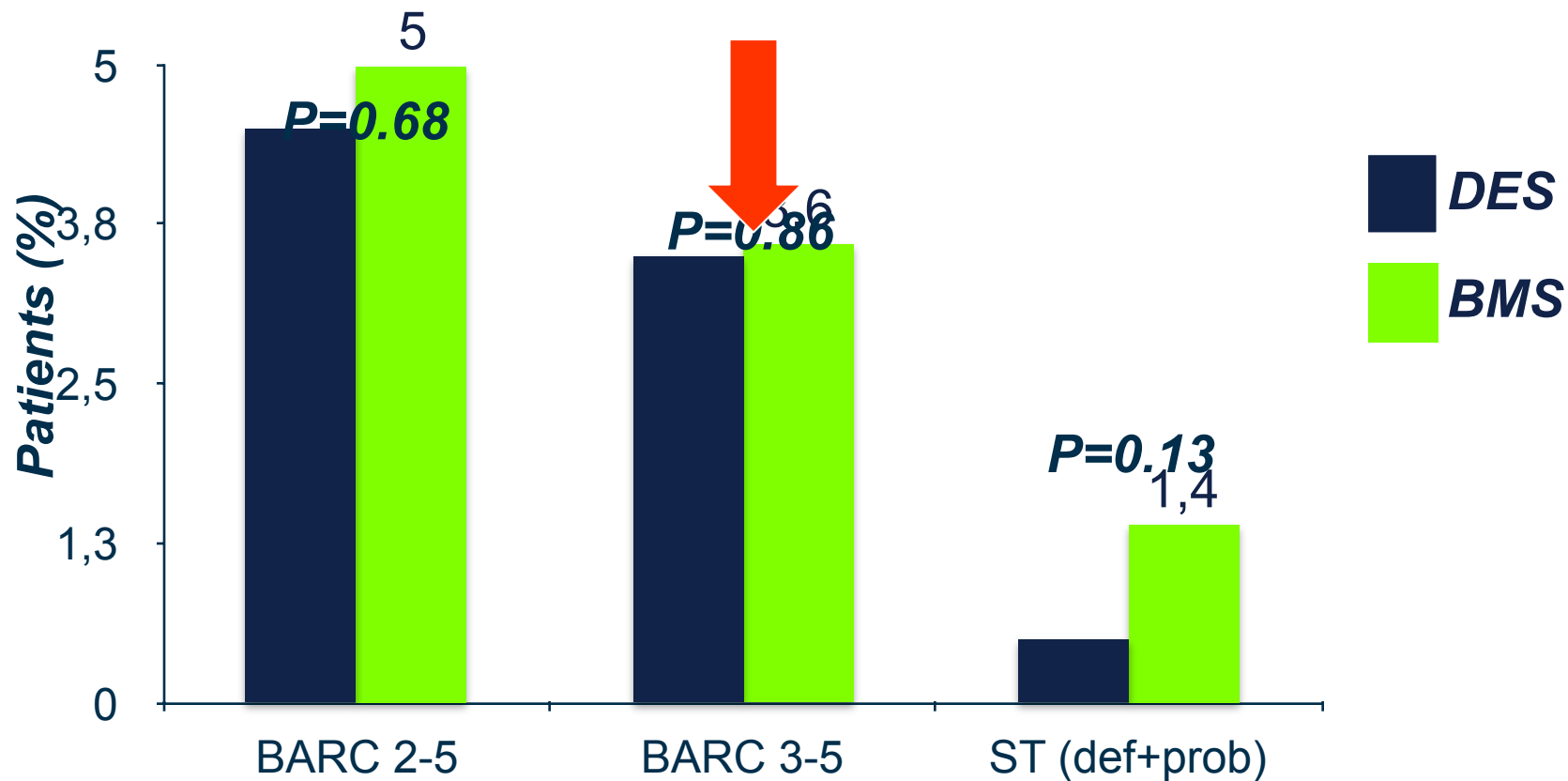
SENIOR

Primary End Point

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



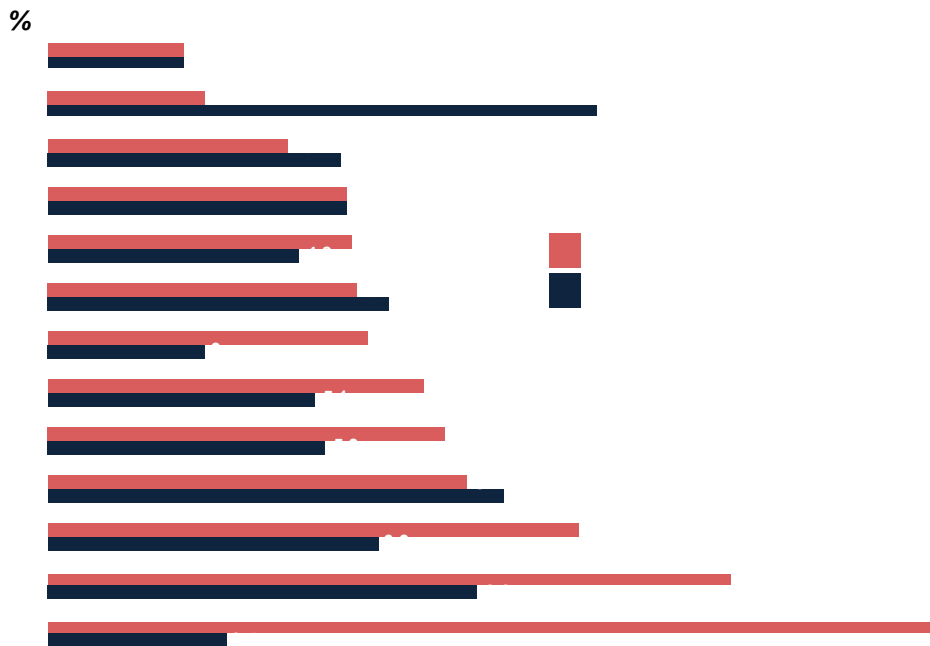
Safety Endpoints



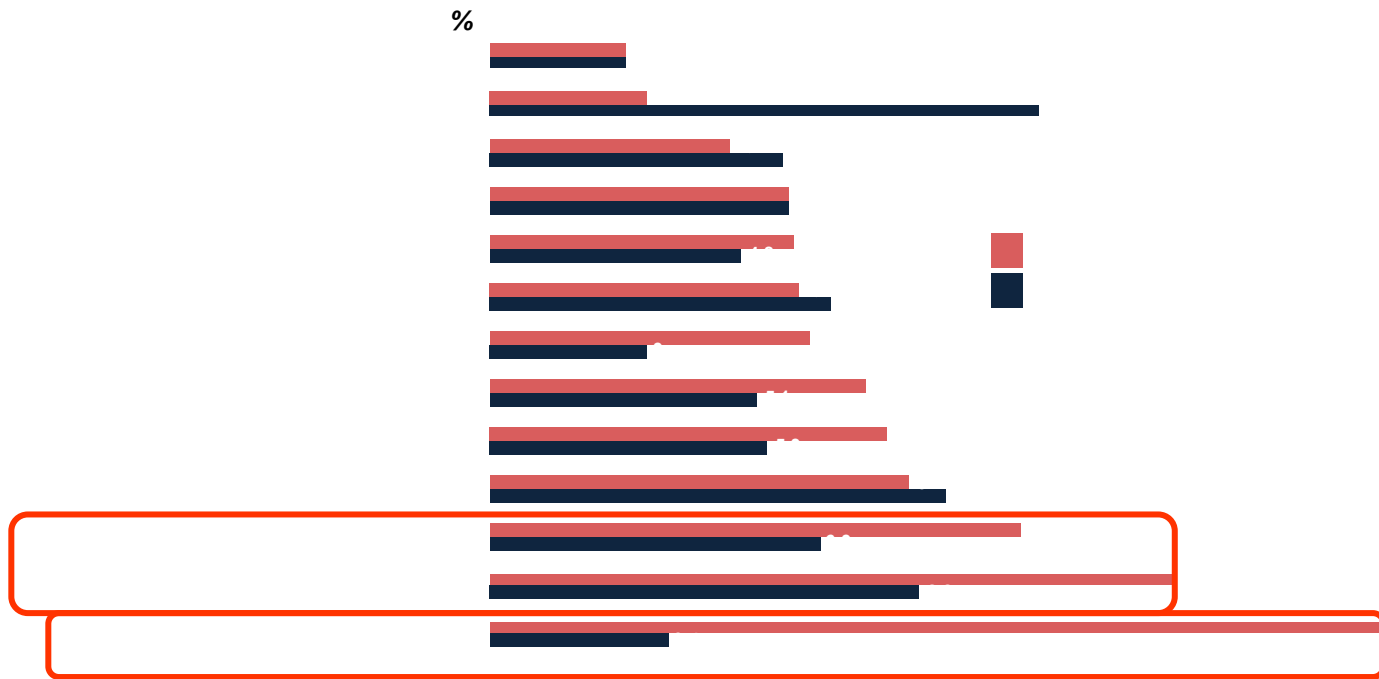
Patients « HBR »

- **Des critères of HBR sont également prédicteurs d'événements thrombotiques.....**

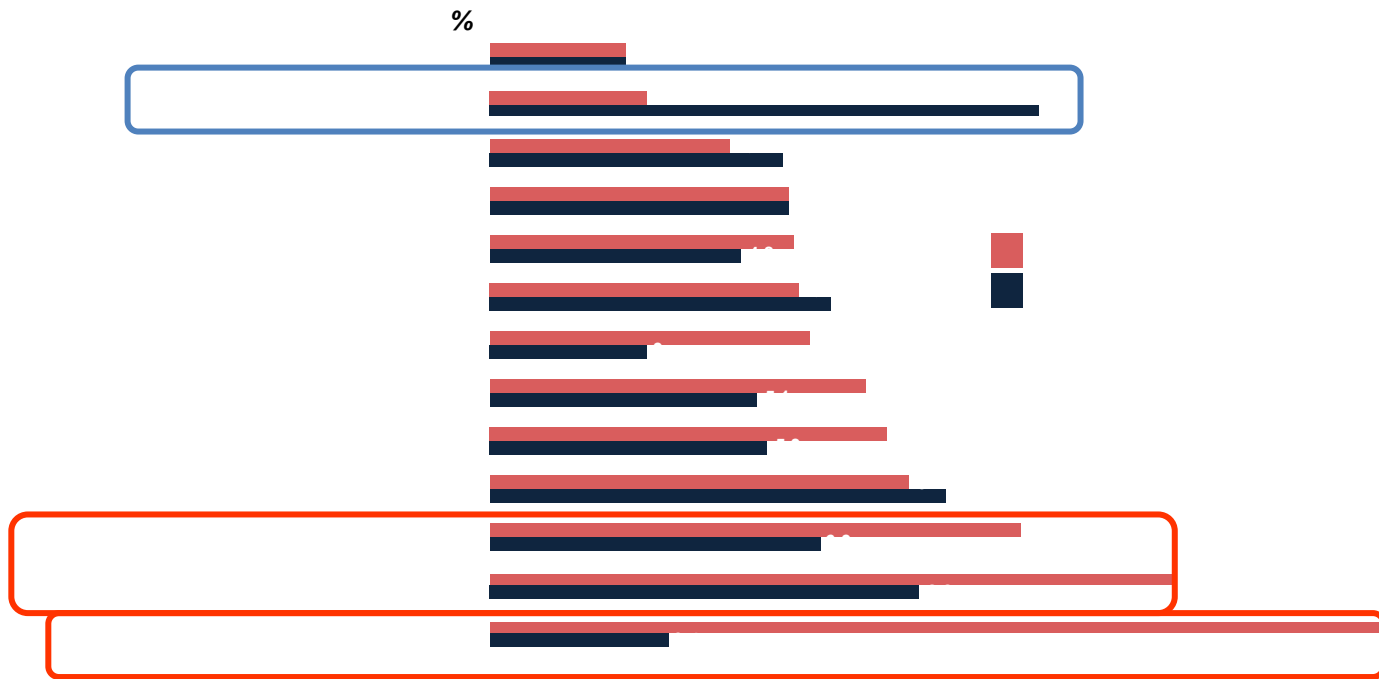
First coronary thrombotic or major bleeding events according to LEADERS FREE inclusion criteria*



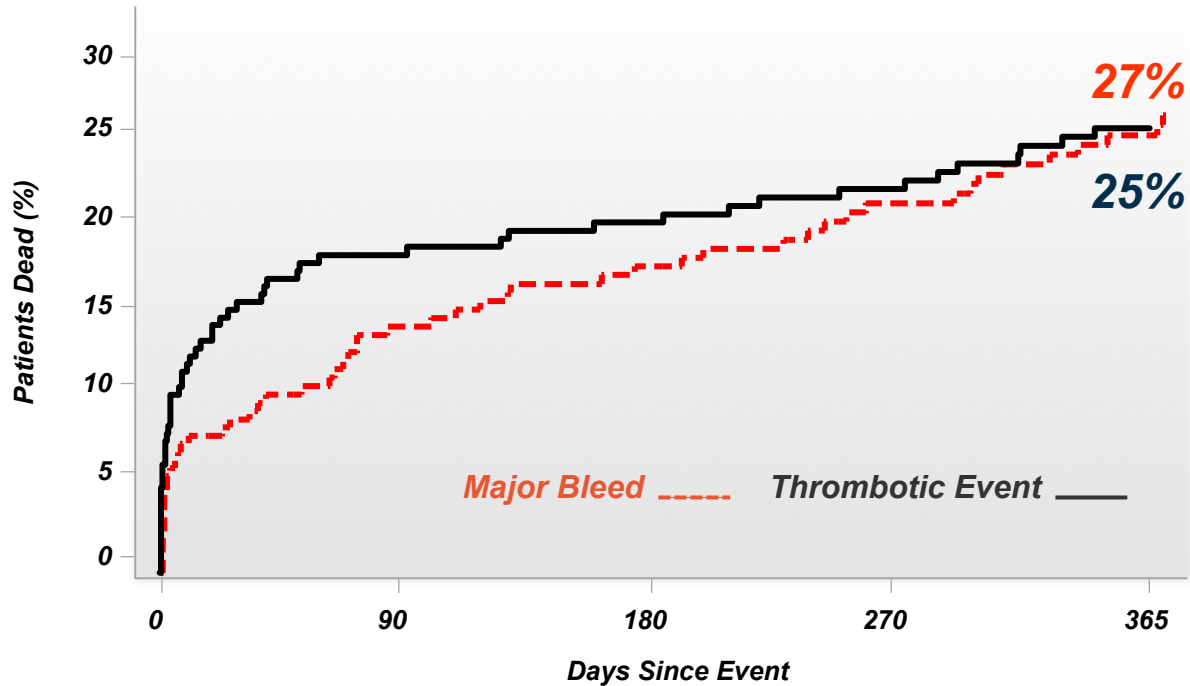
First coronary thrombotic or major bleeding events according to LEADERS FREE inclusion criteria*



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

Les patients HBR

- **Est-ce que les scores nous aident?**

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 ¹⁸	DAPT score ¹⁵
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 ^a	<p>HB ≥ 12 11.5 11 10.5 ≤ 10</p> <p>WBC ≤ 5 8 10 12 14 16 18 ≥ 20</p> <p>Age ≤ 50 60 70 80 ≥ 90</p> <p>CrCl ≥ 100 80 60 40 20 0</p> <p>Prior Bleeding No <input type="checkbox"/> Yes <input type="checkbox"/></p> <p>Score Points 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30</p>	<p>Age ≥ 75 -2 pt 65 to <75 -1 pt <65 0 pt Cigarette smoking +1 pt Diabetes mellitus +1 pt MI at presentation +1 pt Prior PCI or prior MI +1 pt Paclitaxel-eluting stent +1 pt Stent diameter <3 mm +1 pt CHF or LVEF <30% +2 pt Vein graft stent +2 pt</p>
Score range	0 to 100 points	-2 to 10 points
Decision making cut-off suggested	Score ≥ 25 → Short DAPT Score <25 → Standard/long DAPT	Score ≥ 2 → Long DAPT Score <2 → Standard DAPT
Calculator	www.precisedaptscore.com	www.daptstudy.org

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,^a Roxana Mehran, MD,^a Gennaro Giustino, MD,^a David J. Cohen, MD, MSc,^b

TABLE 4 Integer Risk Score for Major Bleeding

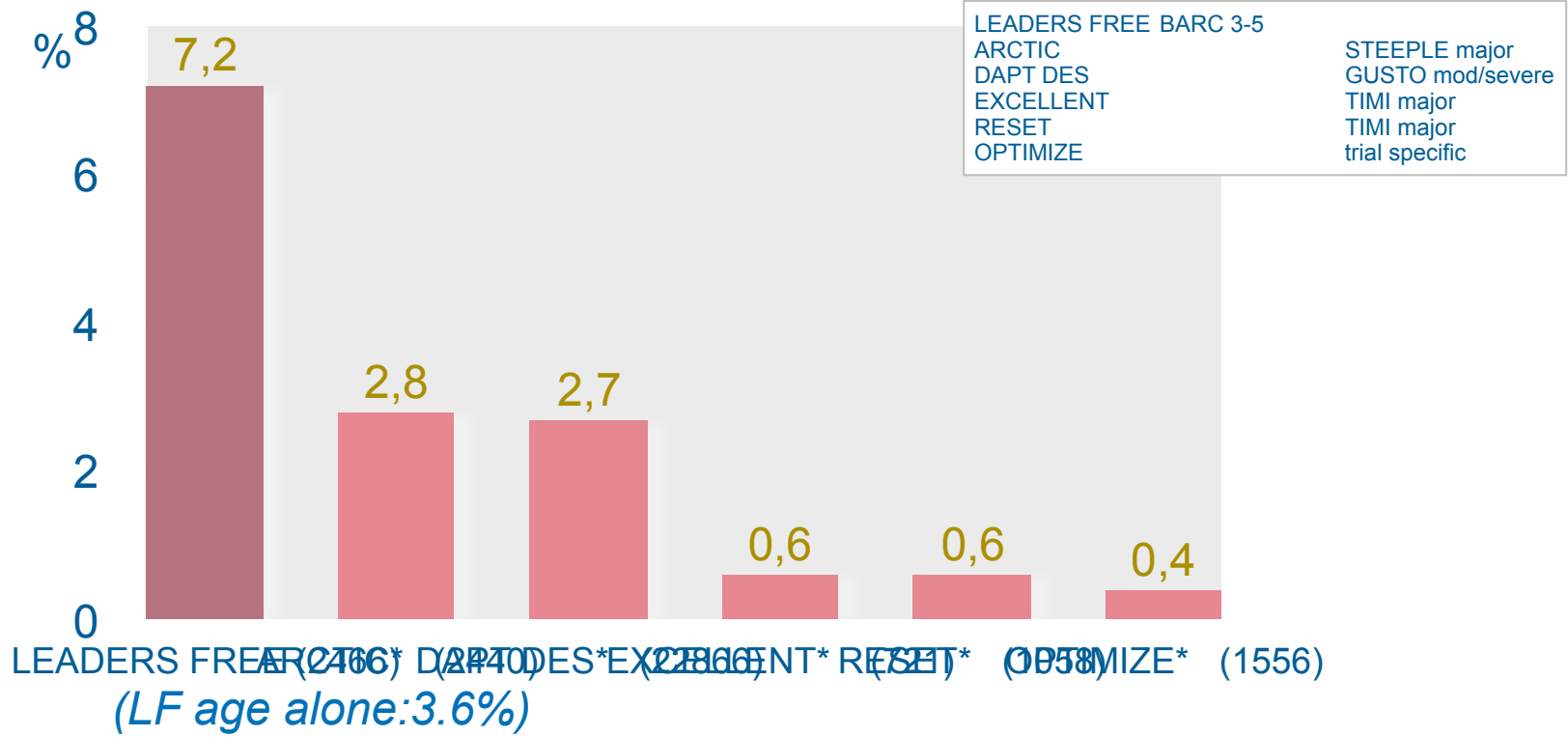
Parameter	Score
Age, yrs	
<50	0
50–59	+1
60–69	+2
70–79	+3
≥80	+4
BMI, kg/m ²	
<25	+2
25–34.9	0
≥35	+2
Current smoking	
Yes	+2
No	0
Anemia	
Present	+3
Absent	0
CrCl <60 ml/min	
Present	+2
Absent	0
Triple therapy on discharge	
Yes	+2
No	0

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



Definition du patient “HBR” questions ouvertes

- * A quel âge devient –on HBR?*
- * Pour les patients sous anticoagulants, quelle durée de DAPT?*
- *Insuffisance rénale comme seul critère?*
- * Cancer (environ 10% dans LF) que traiter en premier?
cancer? Coronaire?*
- *doit on se servir des scores?si oui lequel?*
- *Quelle est la durée optimale de DAPT pour les patientsHBR?*

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

**Stent Ultimaster,
4300 HBR pts,
110 sites, 60 countries,
near 1500 pts already 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, next (last) in Paris in October 2018

Au total, les questions sans réponse à ce jour :

Identifier les patients à haut risqué de saignement

Scores ou bon sens Clinique? En tous cas un score dédié à la population est indispensable

L'age et les anticoagulants oraux sont les 2 plus frequents, mais il y en a de nombreux autres, c'est la tache que s'est assignée le groupe ARC HBR

Strategies dédiées pour cette population HBR

Des devices dédiés? Les stents nus sont "out", est ce que toutes les dernières générations de DES sont déconnectés de la durée du traitement antiplaquettaire?

Merci de votre attention!