INSTITUT CARDIOVASCULAIRE PARIS SUD

www.icps.fr

Faut il avoir peur du patient à haut risque hémorragique?

Réduire le risque et la durée de la DAPT: comment faire?

P. Garot, Institut Cardiovasculaire Paris-Sud

Disclosures

- Speaker fees: Abbott, Biosensors, Boston Scientific, Edwards
- Stockholder and medical co-director Cardiovascular European Research Center

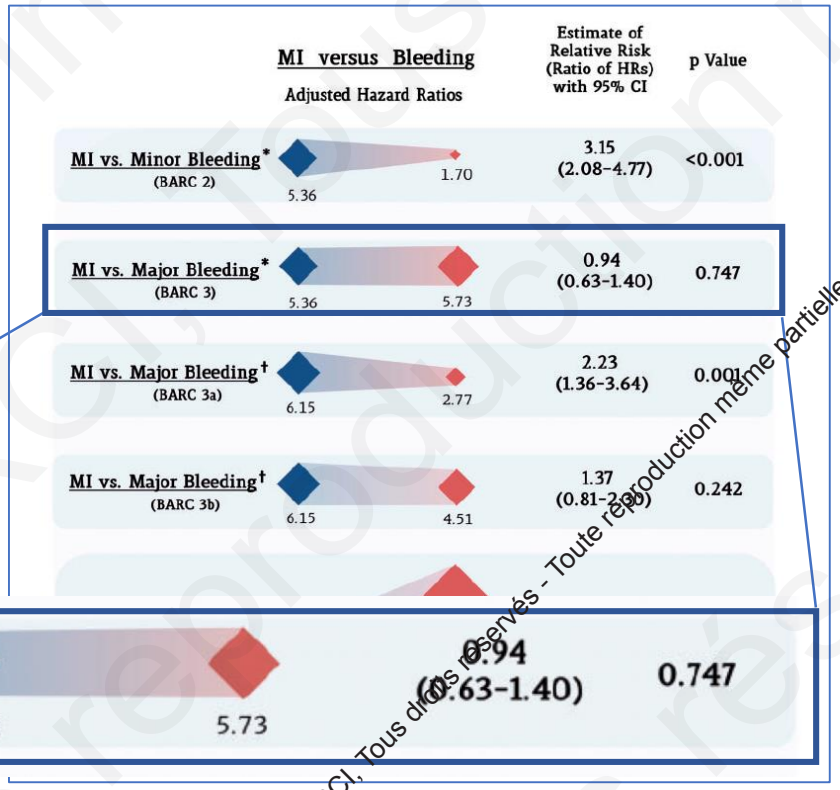
2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.
2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.

Does bleeding really matter?

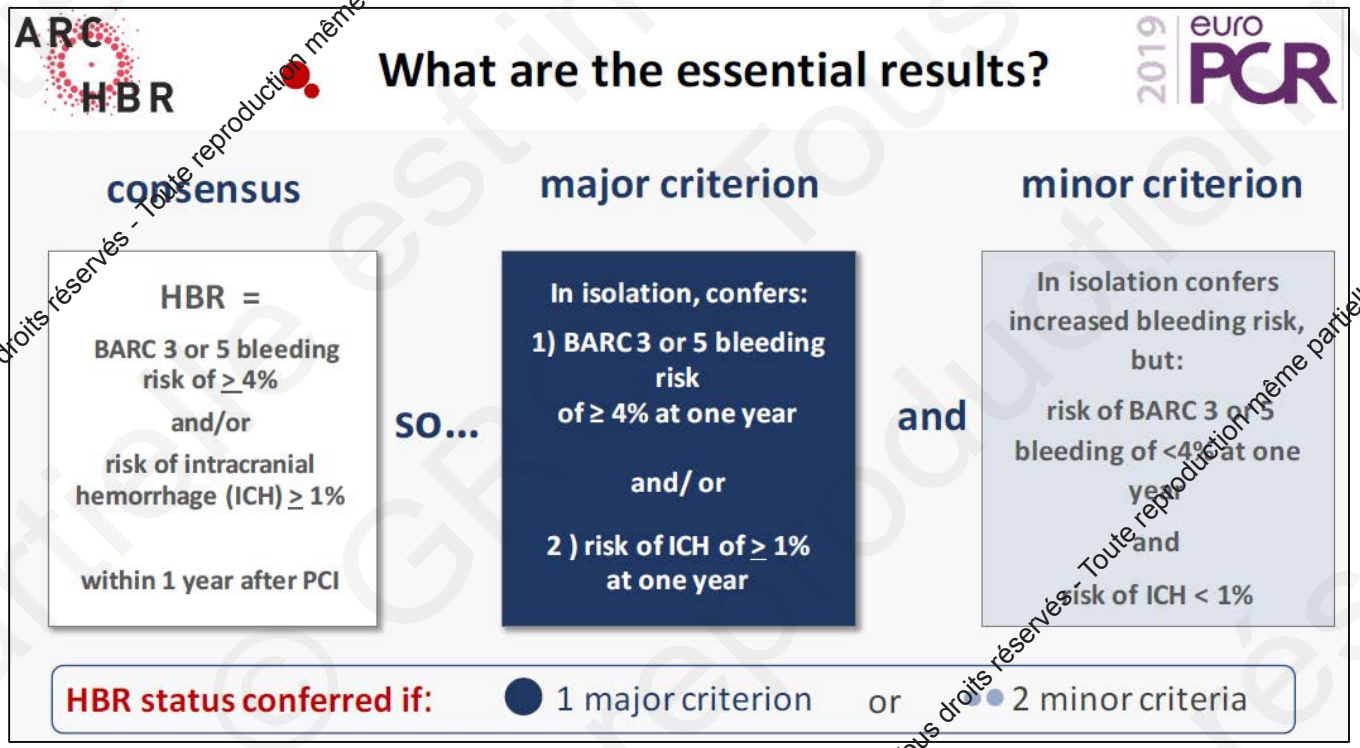
Trade-off of myocardial infarction vs. bleeding types on mortality after acute coronary syndrome: lessons from the Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome (TRACER) randomized trial

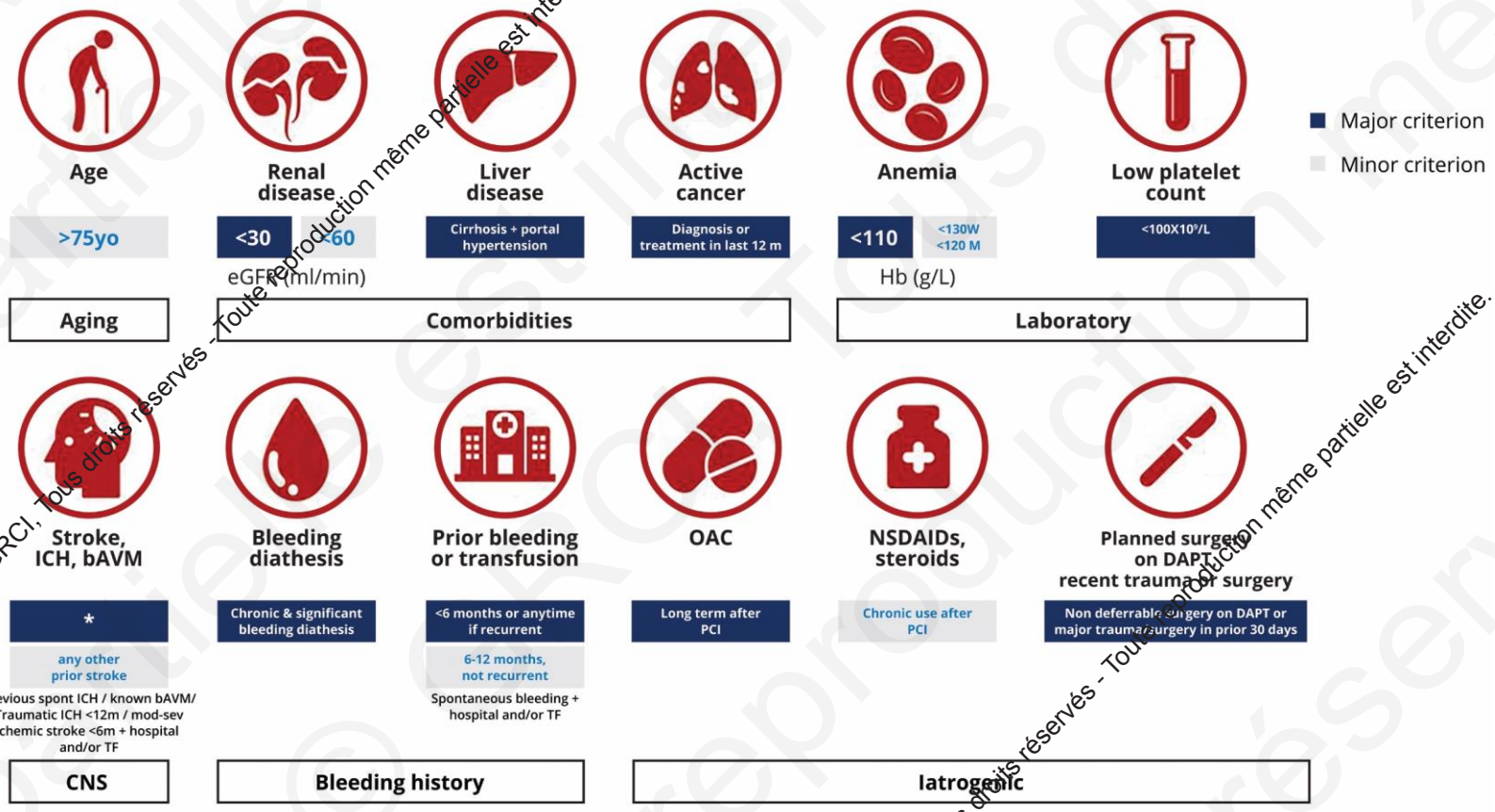
Marco Valgimigli[1,2*], Francesco Costa[2,3], Yuliya Lokhnygina[4], Robert M. Clare[4], Lars Wallentin[5], David J. Moliterno[6], Paul W. Armstrong[7], Harvey D. White[8], Claes Held[5], Philip E. Aylward[9], Frans Van de Werf[10], Robert A. Harrington[11], Kenneth W. Mahaffey[11], and Pierluigi Tricoci[4]

- 12702 NSTEMI patients
- Enrolled in TRACER (vorapaxar vs control)
- MI & bleeding > 30 days post ACS
- Mortality versus MI or BARC bleed



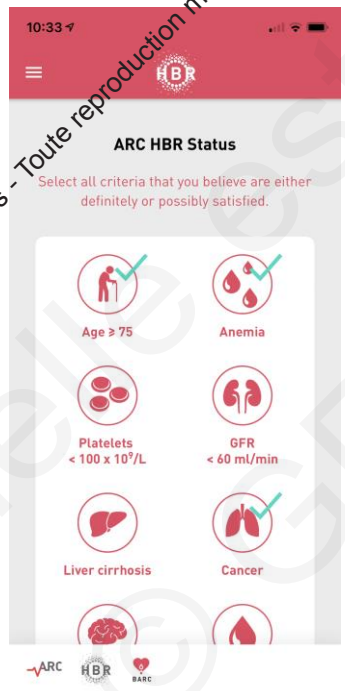
Identify HBR patients
ARC HBR Initiative

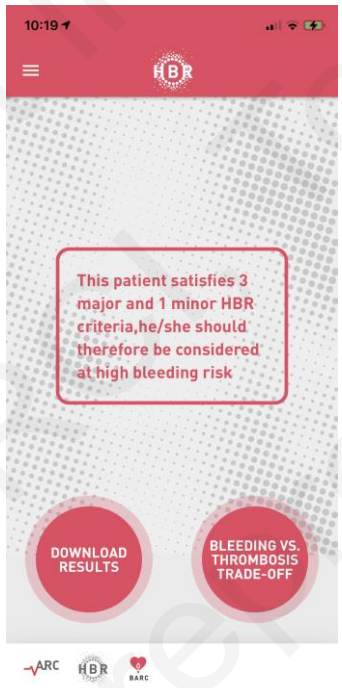


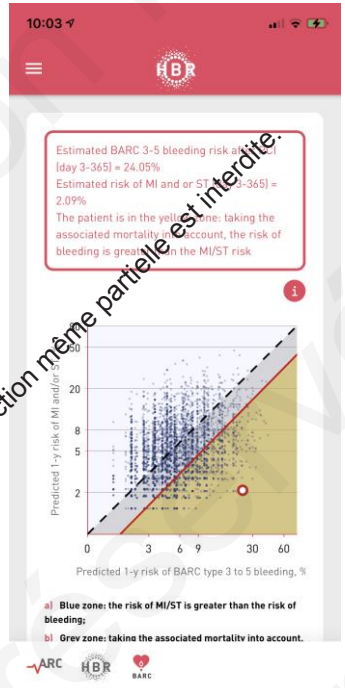


P. Urban. Defining high bleeding risk in patients undergoing PCI: a consensurs from the Academic Research Consortium for high bleeding risk - EuroPCR oral presentation

App

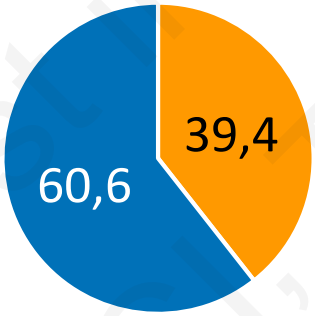




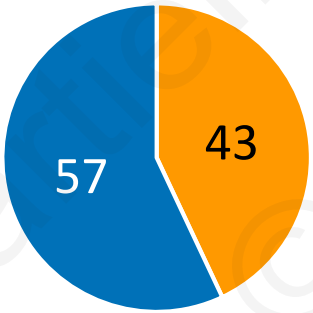


Prevalence of ARC-HBR patients in PCI registries

Ueki et al [2]

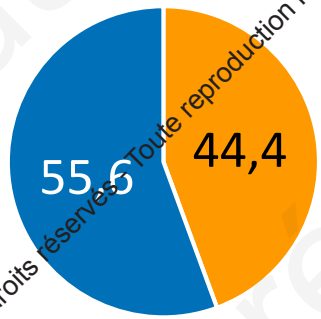


Natsuaki et al [1]



ARC HBR non-HBR

Cao et al [3]



1. Circ Cardiovasc Interv. 2019;12:e008307
2. EuroIntervention 2020;16:371-379
3. JACC 2020; 75:2711-22

Non invasive testing if applicable

2019 ESC Guildelines

New major recommendations in 2019	
Basic testing, diagnostics, and risk assessment	
Non-invasive functional imaging for myocardial ischaemia or coronary CTA is recommended as the initial test for diagnosing CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.	I
It is recommended that selection of the initial non-invasive diagnostic test be based on the clinical likelihood of CAD and other patient characteristics that influence test performance, local expertise, and the availability of tests.	I
Functional imaging for myocardial ischaemia is recommended if coronary CTA has shown CAD of uncertain functional significance or is not diagnostic.	I
Invasive angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood and severe symptoms refractory to medical therapy, or typical angina at a low level of exercise and clinical evaluation that indicates high event risk. Invasive functional assessment must be available and used to evaluate stenoses before revascularization, unless very high grade (>90% diameter stenosis).	I
Invasive coronary angiography with the availability of invasive functional evaluation should be considered for confirmation of the diagnosis	

Invasive angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood and severe symptoms refractory to medical therapy, or typical angina at a low level of exercise and clinical evaluation that indicates high event risk. Invasive functional assessment must be available and used to evaluate stenoses before revascularization, unless very high grade (>90% diameter stenosis). I

2013	Class[a]	2019	Class[a]
Exercise ECG is recommendedas the initial test to establish a diagnosis of stable CAD in patients withsymptoms of angina and intermediate PTP of CAD (15–65%), free of anti-ischaemic drugs, unless they cannot exercise or display ECG changes that make the ECG non-evaluable.	I	Exercise ECG is recommended for the assessment of exercise tolerance, symptoms, arrhythmias, BP response, and event risk in selected patients.	I
		Exercise ECG may be considered as an alternative test to rule-in or rule-out CAD when other non-invasive or invasive imaging methods are not available.	IIb
Exercise ECG should be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIa	Exercise ECG may be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIb

Knuuti J, et al. Eur Heart J (2019) 00, 1–71.

Non invasive testing if applicable

ESTABLISHING PRE TEST PROBABILITY OF CAD

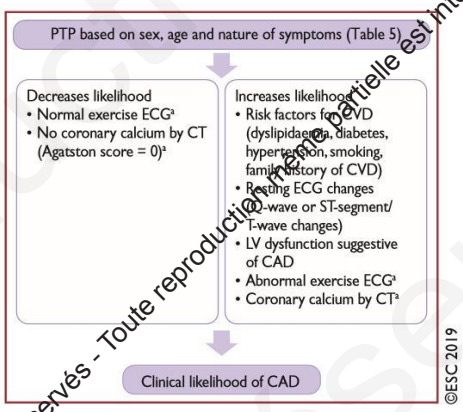
- **DIAMOND AND FORRESTER (based on sex, age, symptoms)**

Table 5 Pre-test probabilities of obstructive coronary artery disease in 15 815 symptomatic patients according to age, sex, and the nature of symptoms in a pooled analysis[64] of contemporary data[7,8,62]

	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

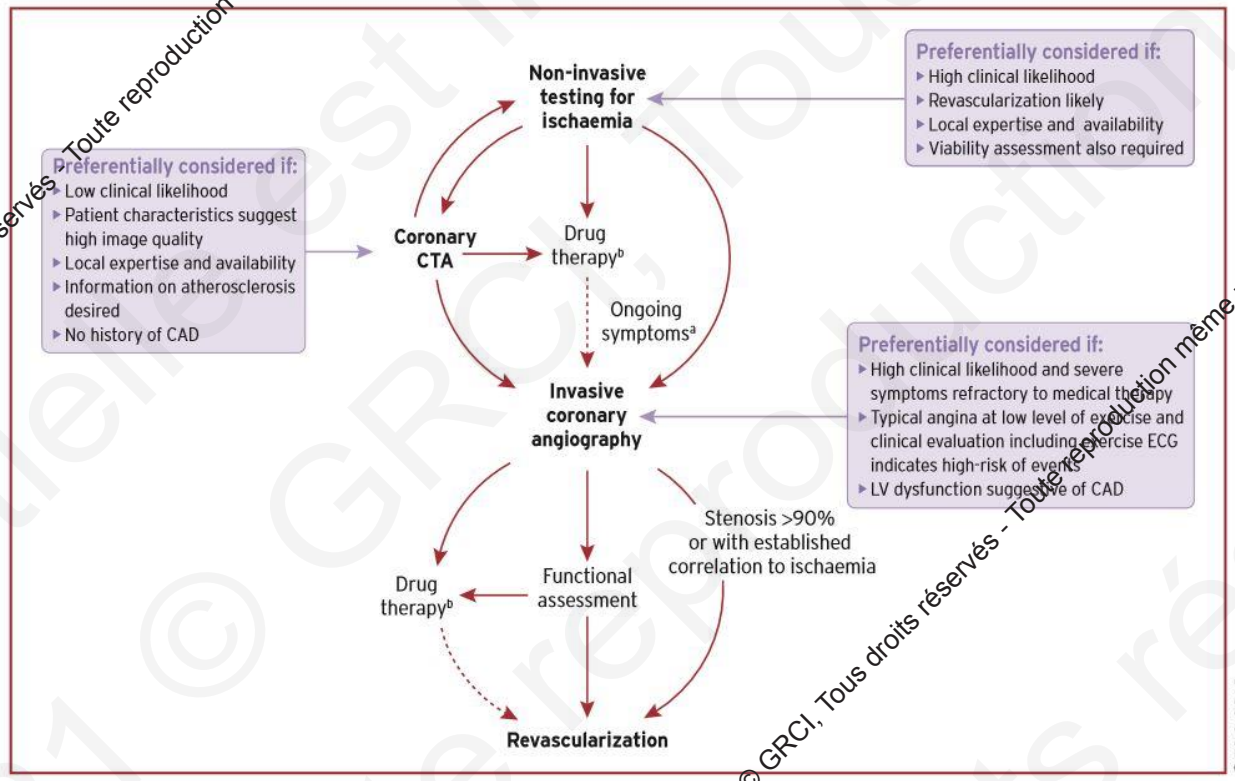
©ESC 2019

CLINICAL LIKELIHOOD of CAD



2019 ESC Guidelines on CCS

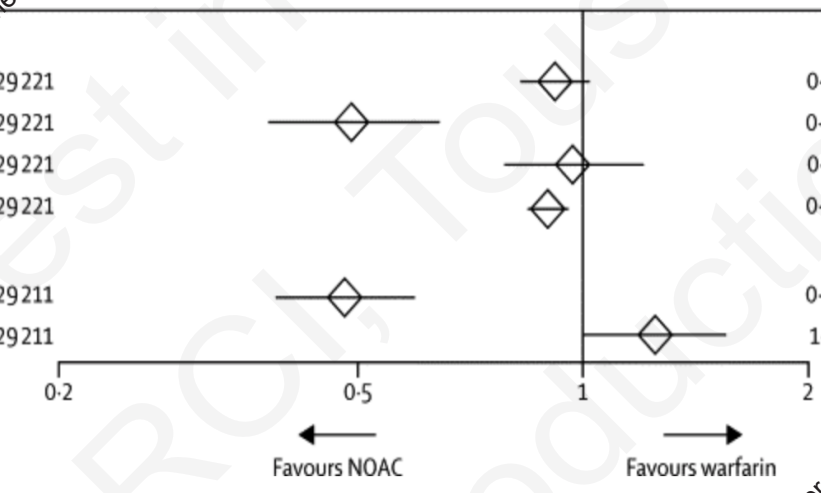
The choice of the test depends on the clinical likekihood of CAD, local expertise and availability

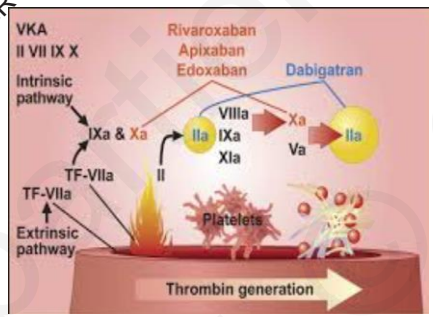


Knuuti J, et al. Eur Heart J (2019) 00, 1–71.

Optimal anticoagulation

	Pooled NOAC (events)	Pooled warfarin (events)	RR (95% CI)	p
Efficacy				
Ischaemic stroke	665/29 292	724/29 221	0·92 (0·83–1·02)	0·10
Haemorrhagic stroke	130/29 292	263/29 221	0·49 (0·38–0·64)	<0·0001
Myocardial infarction	413/29 292	432/29 221	0·97 (0·78–1·20)	0·77
All-cause mortality	2022/29 292	2245/29 221	0·90 (0·85–0·95)	0·0003
Safety				
Intracranial haemorrhage	204/29 287	425/29 211	0·48 (0·39–0·59)	<0·0001
Gastrointestinal bleeding	751/29 287	591/29 211	1·25 (1·01–1·55)	0·043





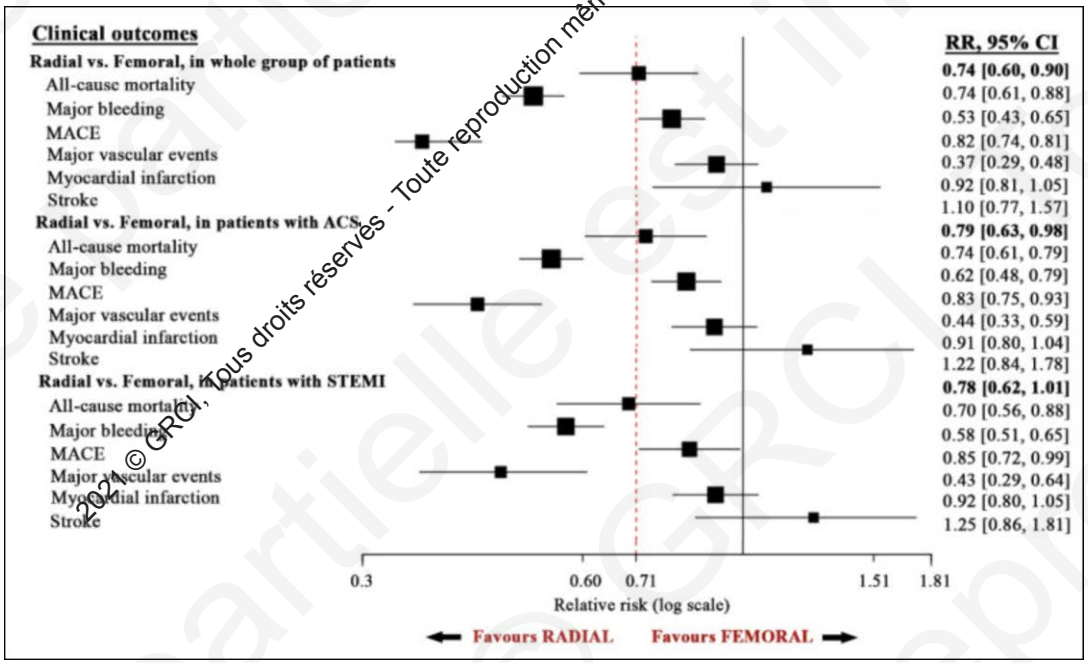
Direct OAC Vs. Warfarin: meta-analysis of RCT

RE-LY, ROCKET-AF, ARISTOTLE, ENGAGE AF-TIMI 48

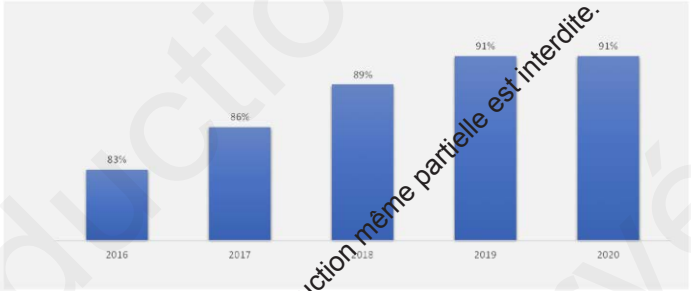
Ruff CT et al. Lancet 2014;383:955-962.

Radial access

34 RCT, 29,352 Pts



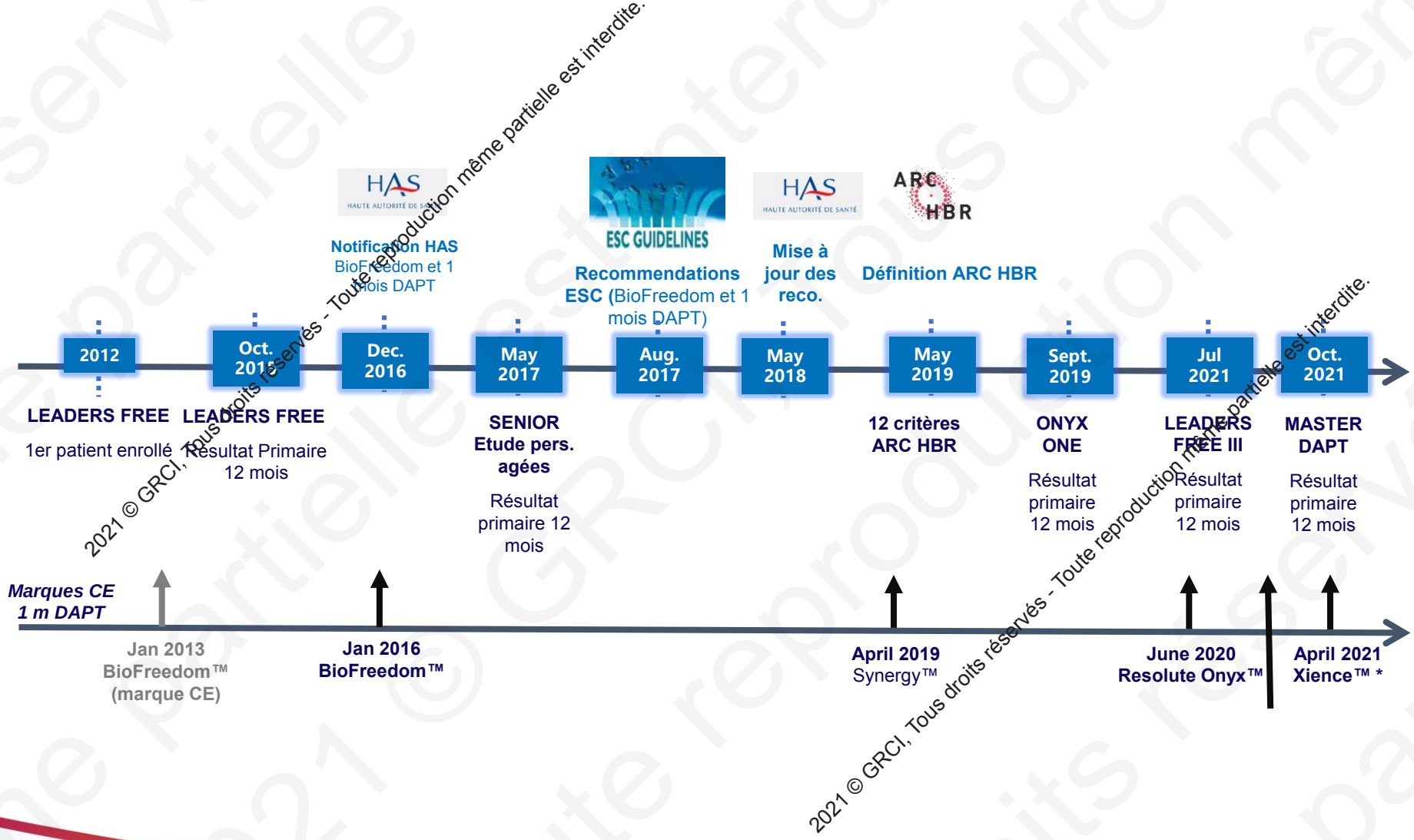
Utilisation de la Radiale (angioplasties)



D. Blanchard High Tech 2021

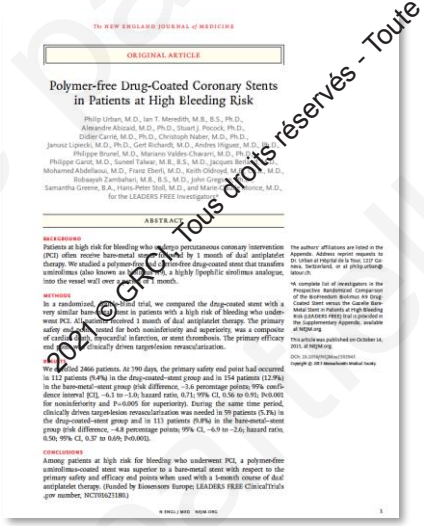
Bajraktari G et al. Lancet 2014;383:955-962.

Appropriate stent selection



4 completed & published randomized trials of short DAPT for HBR patients

BioFreedom DCS vs. BMS (1 month)



LEADERS FREE

Endeavor ZES vs. BMS (1 month)

ZEUS HBR

Synergy EES vs. BMS (1 or 6 months

SENIOR

Onyx ZES vs. BF-DCS (1 month)

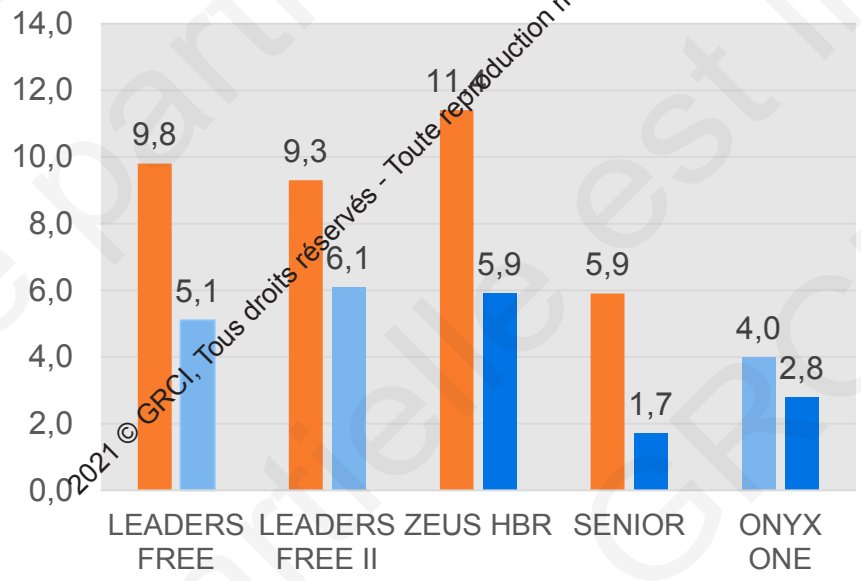
ONYX-ONE

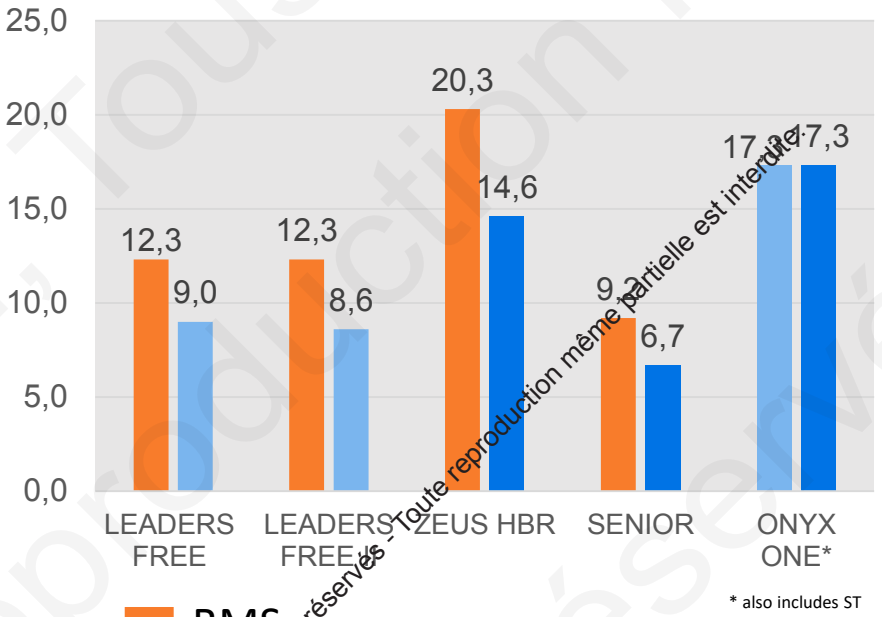
11 other trials of ≤3 months DAPT for HBR patients

	trial	stent	type	limus kinetics	patients	experimental arm DAPT	control arm DAPT	status May 2020
randomized	COBRA-REDUCE	Cobra PzF	Polyzene-F nanocoating	na	840 on AVK or NOAC	2 weeks	EES or R-ZES & 6 months DAPT	enrolling
	MASTER DAPT	Ultimaster SES	2nd G BD polymer	slow	4300 HBR	1 month	guidelines	follow-up
	TARGET SAFE	Firehawk	Biodegradable polymer	slow	1700 HBR	1 month	6 months	enrolling
single arm	**LEADERS FREE II**	**BioFreedom DCS**	**Polymer free**	**fast**	**1200 HBR**	**1 month**	**BMS arm of LEADERS FREE**	**Completed Circ interv 2020**
	EVOLVE SHORT DAPT	Synergy EES	2nd G BD polymer	slow	2000 HBR	3 months	historical group (12 months) & OPC	Presented TCT 2019
	POEM	Synergy EES	2nd G BD polymer	slow	1023 HBR	1 month	single arm trial	enrolling
	XIENCE 90	Xience EES	Permanent polymer	slow	2000 HBR	3 months	single arm trial	follow-up
	XIENCE Global 28	Xience EES	Permanent polymer	slow	960 HBR	1 month	single arm trial	follow-up
	XIENCE 28 USA	Xience EES	Permanent polymer	slow	800 HBR	1 month	single arm trial	follow-up
	ONYX ONE CLEAR	Resolute Onyx DES	Permanent polymer	slow	800 HBR	1 month	performance goal	Presented ACC 2020
	LEADERS FREE III	CoCr BioFreedom	Polymer-free	fast	1200 HBR	1 month	DCS arm of LEADERS FREE	Planned presentation Euro-PCR 2020

2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.
2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.

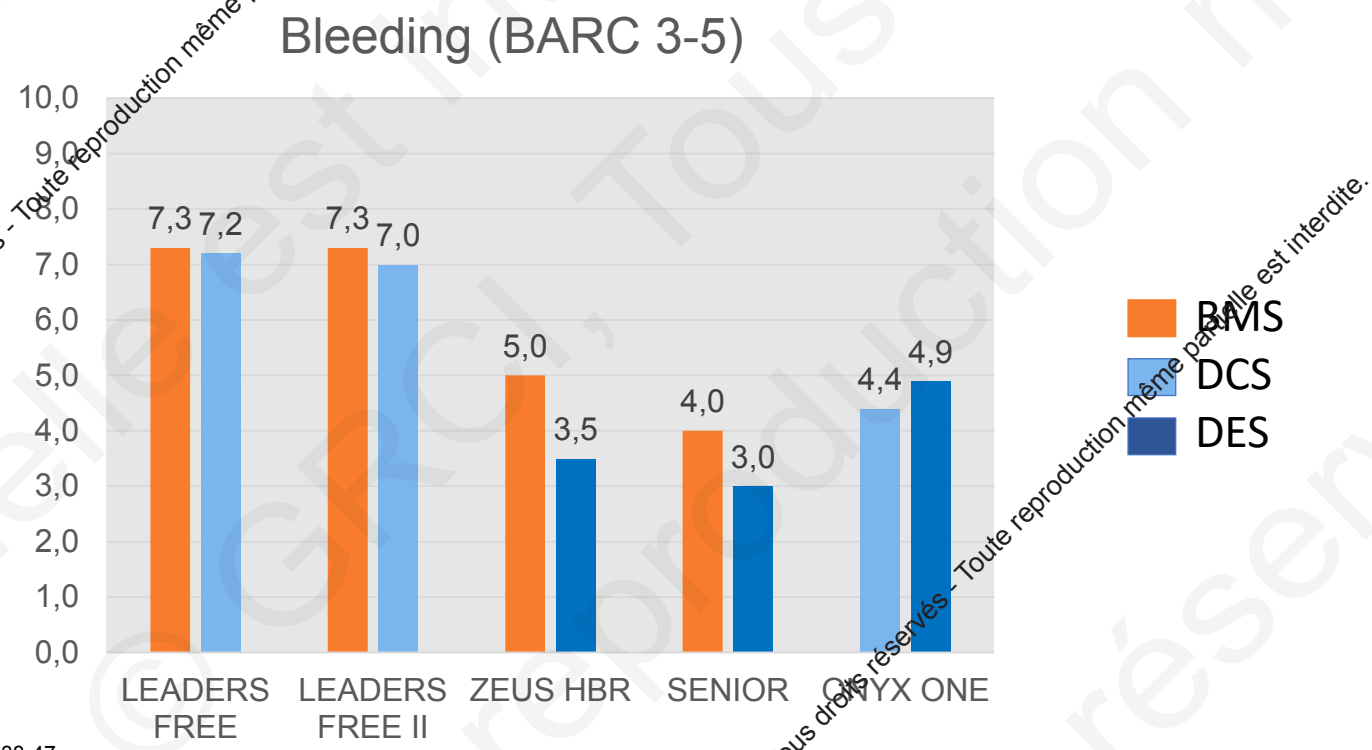
LEADERS FREE I & II, ZEUS HBR, SENIOR & ONYX ONE





Urban P et al, N Engl J Med 2015;373:2038-47
Ariotti S et al, JACC interv 2016; 9: 426-36
Varenne O et al, Lancet 2017; 391: 41-50
Windecker S et al, N Engl J Med 2020; DOI: 10.1056/NEJMoa1910021
Krucoff M et al, Circ Cardiovasc Interv doi: 10.1161/CIRCINTERVENTIONS.119.008603

LEADERS FREE I & II, ZEUS HBR, SENIOR & ONYX ONE



Urban P et al, N Engl J Med 2015;373:2038-47
Ariotti S et al, JACC interv 2016; 9: 426-36
Varenne O et al, Lancet 2017; 391: 41-50
Windecker S et al, N Engl J Med 2020; DOI: 10.1056/NEJMoa1910021
Krucoff M et al, Circ Cardiovasc Interv doi: 10.1161/CIRCINTERVENTIONS.119.008603

DAPT ESC Guidelines – Last online update 2018

Dual antiplatelet therapy duration in high bleeding risk patients with stable coronary artery disease treated with percutaneous coronary intervention

ESC European Society of Cardiology

Recommendations	Class	Level
In patients with stable CAD considered at high bleeding risk (e.g. PRECISE-DAPT ≥25), DAPT for 3 months should be considered[1].	IIa	B
In patients with stable CAD in whom 3-month DAPT poses safety concerns, DAPT for 1 month may be considered[2].	IIb	C

[1]:The evidence supporting this recommendation comes from two studies where zotarolimus-eluting Endeavour sprint stent has been investigated in conjunction with a 3-month DAPT regimen.

[2]:1-month DAPT after implantation of zotarolimus-eluting Endeavour sprint stent or drug coated Biofreedom stent reduced risks of reintervention, myocardial infarction and inconsistently of stent thrombosis compared to bare-metal stent under similar DAPT duration.
It is unclear if this evidence applies to other contemporary DES.

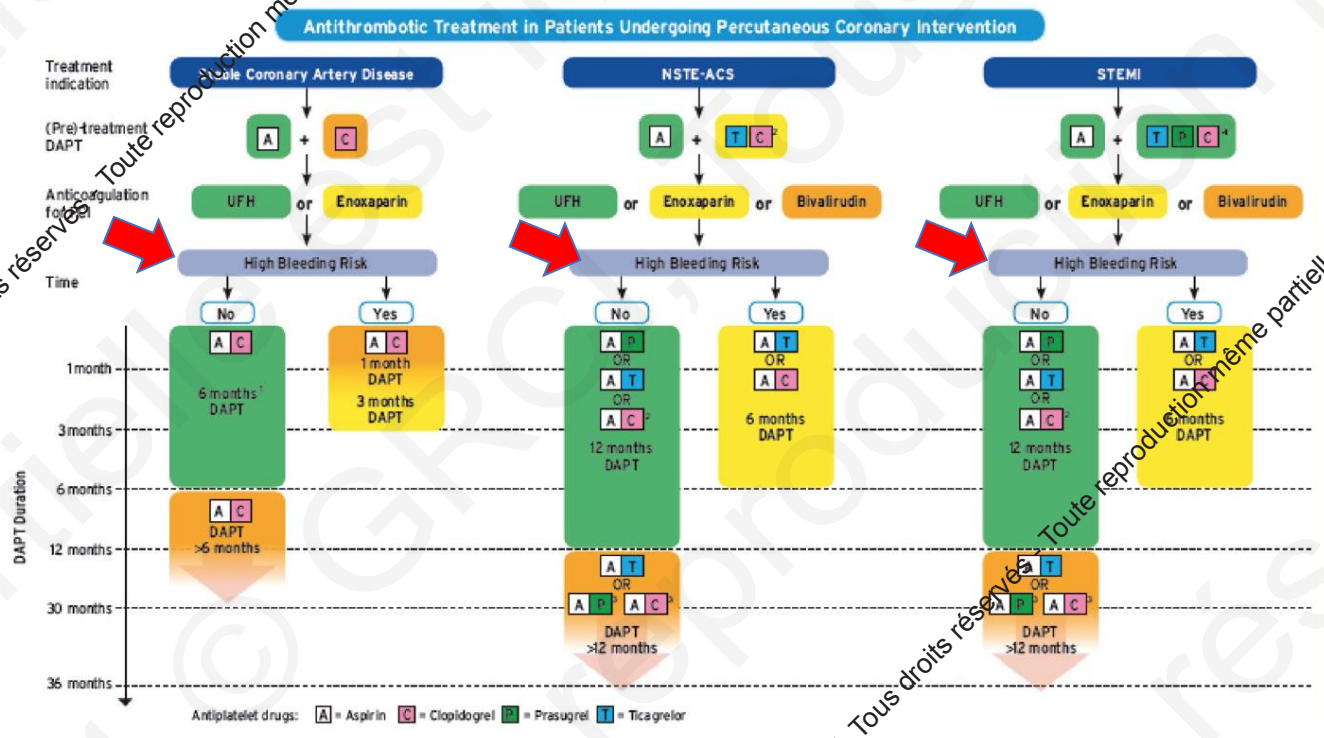
www.escardio.org/guidelines

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

6

2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.
2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.

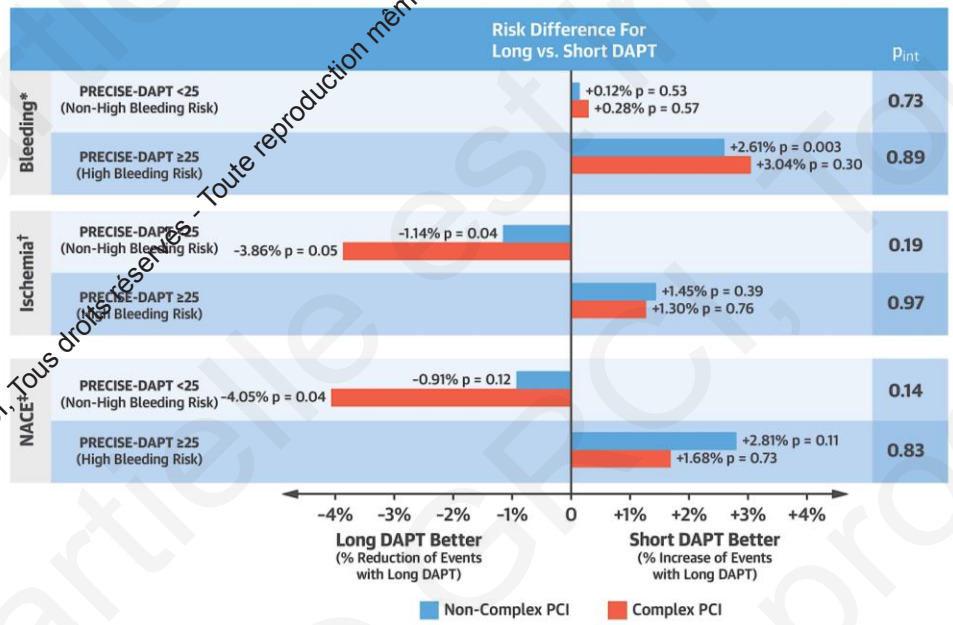
2018 ESC/EACTS Guidelines on myocardial revascularization



Neuman F-J et al. European Heart Journal 2018 doi:10.1093/eurheartj/ehy394

IPL meta-analysis of 14,963 patients from 8 trials of DAPT duration

DAPT, complexity and the PRECISE-DAPT score



COMPLEX PCI

Long DAPT increases bleeding if PRECISE-DAPT ≥25 (HBR)

Long DAPT reduces MACE in complex PCI if PRECISE-DAPT <25 (non-HBR)

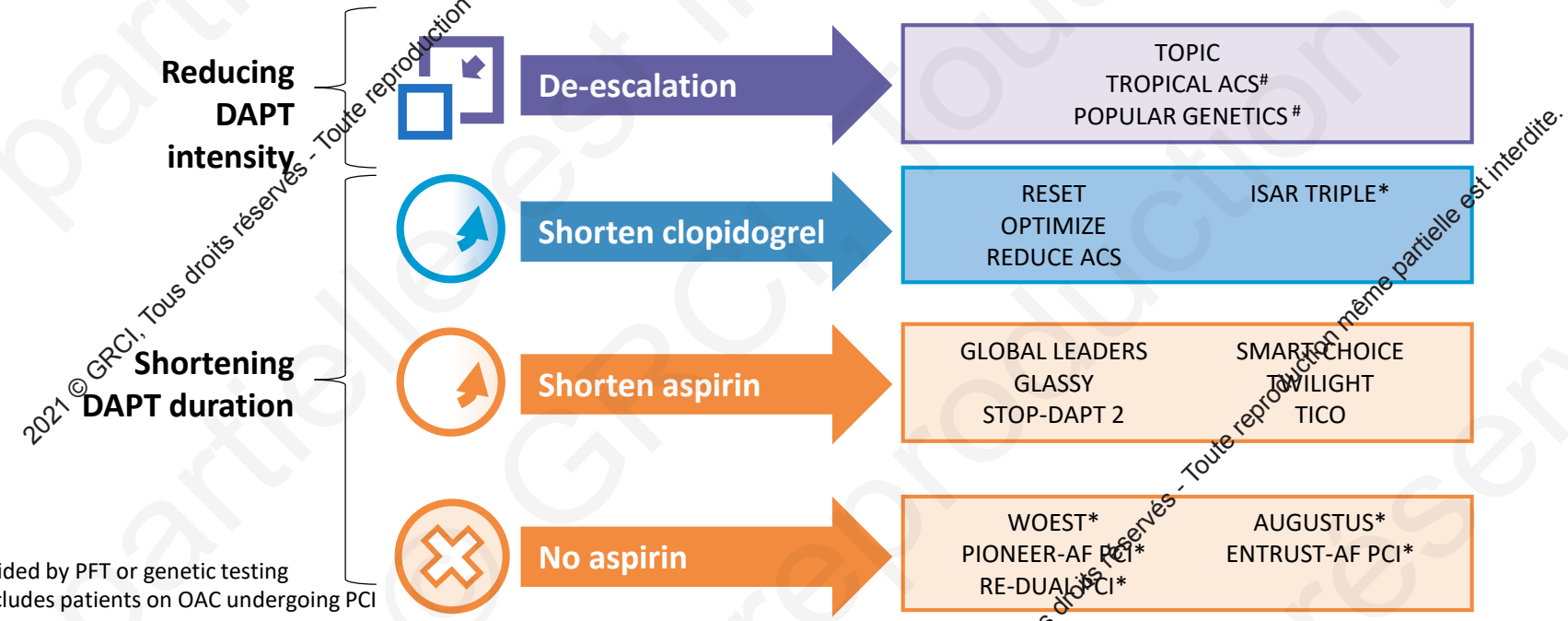
NET BENEFIT
Non-HBR: long DAPT better
HBR: short DAPT better

Complex PCI was defined as having at least 1 of the following features: 3 vessels treated, ≥3 stents implanted, ≥3 lesions treated, bifurcation with 2 stents implanted, total stent length >60 mm, or CTO

Short DAPT: 3 or 6 months; Long DAPT: 12 or 24 months

Can we do any better for PCI patients on DAPT?

Strategies to reduce bleeding after PCI



Guided by PFT or genetic testing
* Includes patients on OAC undergoing PCI

2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.

2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.

Adapted from Capodanno D et al. J Am Coll Cardiol. 2020;76:1468-1483.

DAPT modulation escalation or de-escalation

Individualized treatment regimen

JACC: CARDIOVASCULAR INTERVENTIONS
© 2019 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

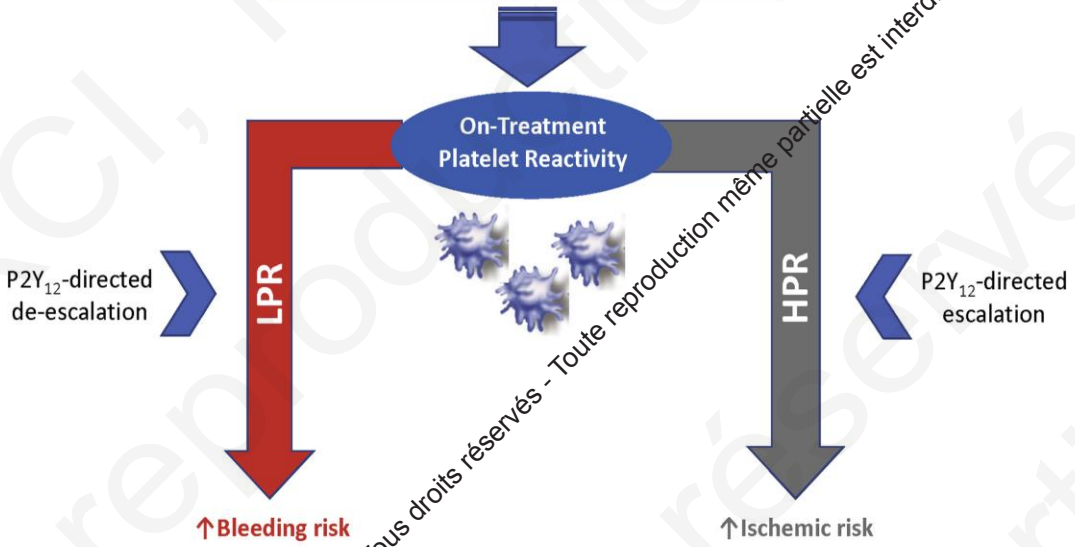
VOL. 12, NO. 16, 2019

STATE-OF-THE-ART REVIEW

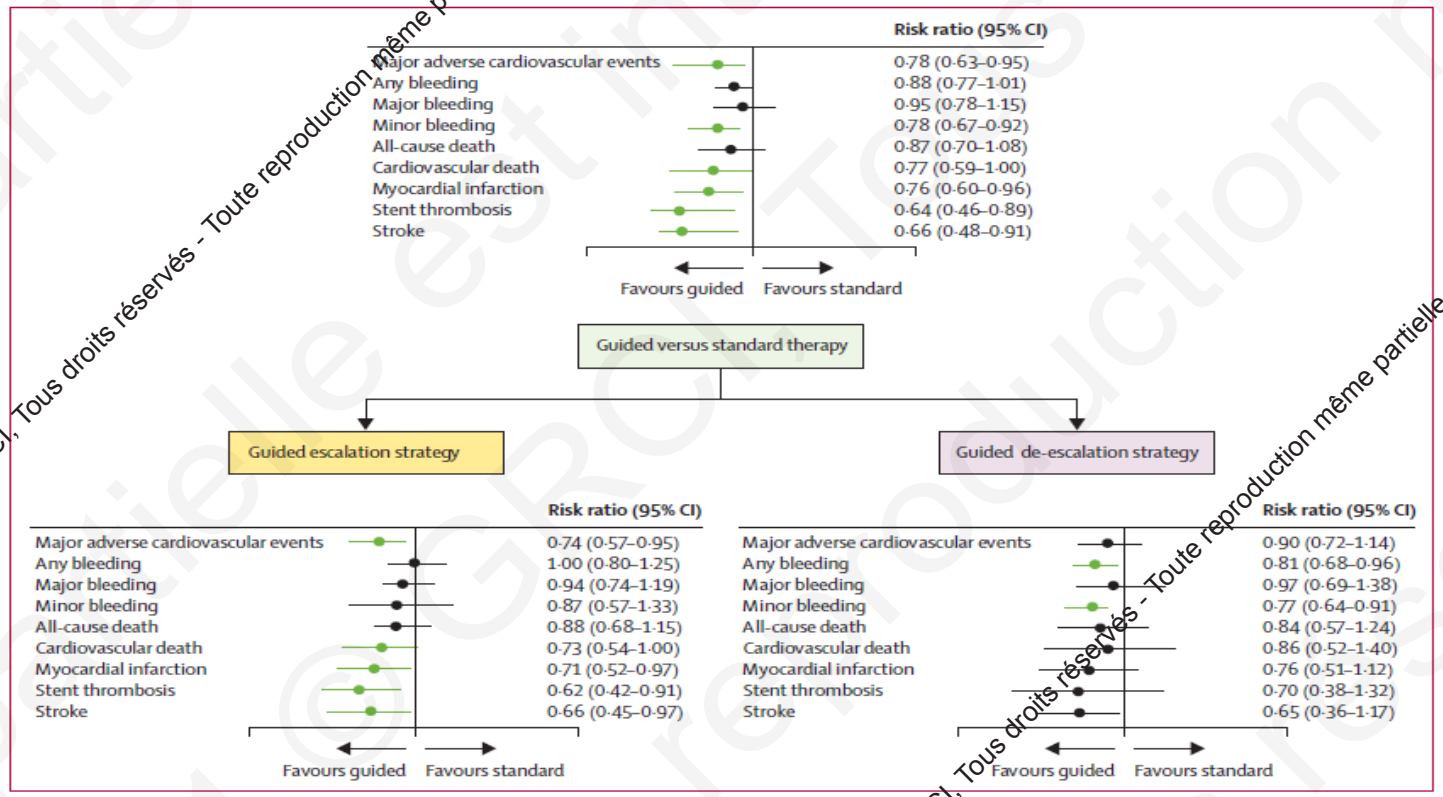
Updated Expert Consensus Statement on Platelet Function and Genetic Testing for Guiding $P2Y_{12}$ Receptor Inhibitor Treatment in Percutaneous Coronary Intervention

Dirk Sibbing, MD, MHBA,[a,b,*] Daniel Aradi, MD, PhD,[c,*] Dimitrios Alexopoulos, MD,[d] Jurrien ten Berg, MD,[e] Deepak L. Bhatt, MD, MPH,[f] Laurent Bonello, MD,[g] Jean-Philippe Collet, MD,[h] Thomas Cuisset, MD,[i] Francesco Franchi, MD,[j] Lisa Gross, MD,[a,b] Paul Gurbel, MD,[k] Young-Hoon Jeong, MD,[l] Roxana Mehran, MD,[m,n] David J. Moliterno, MD,[o] Franz-Josef Neumann, MD,[p] Naveen L. Pereira, MD,[q] Matthew J. Price, MD,[r] Marc S. Sabatine, MD, MPH,[s] Derek Y.F. So, MD,[t] Gregg W. Stone, MD,[u,v] Robert F. Storey, MD,[w] Udaya Tantry, MD,[x] Dietmar Trenk, PhD,[p] Marco Valgimigli, MD,[y] Ron Waksman, MD,[z] Dominick J. Angiolillo, MD, PhD[j]

Modifiable factors:	Non-modifiable factors:
• Diabetes • Smoking • High BMI • Drug interactions • Inflammation	• Genetics (CYP2C19 SNPs) • Age • Sex • CKD



Guided (Platelet Function/Genetic Testing) vs Standard APT in Pts Undergoing PCI: A Systematic Review and Meta-analysis (n=20743)



Galli M, Angiolillo DJ. Lancet 2021; 397: 1470-83

Choice of DAPT – Short DAPT – DAPT modulation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ticagrelor with or without Aspirin in High-Risk Patients after PCI

R. Mehran, U. Baber, S.K. Sharma, D.J. Cohen, D.J. Angiolillo, C. Briguori, J.Y. Cha, T. Collier, G. Dangas, D. Dudek, V. Džavík, J. Escaned, R. Gil, P. Gurbel, C.W. Hamm, T. Henry, A. Huber, A. Kastrati, U. Kaul, R. Kornowski, M. Krucoff, V. Kunadian, S.O. Marx, S.R. Mehta, D. Moliterno, E.M. Ohman, K. Oldroyd, G. Sardella, S. Sartori, R. Shlofmitz, P.G. Steg, G. Weisz, B. Witzenbichler, Y. Han, S. Pocock, and C.M. Gibson

3Mo DAPT Ticagrelor + aspirin
7,119 Randomization after 3Mo
Randomization Aspirin or placebo (+ Ticagrelor for all)
Asymptomatic+stable angina: 2,503Pts (35%)
Unstable angina+NSTEMI: 4,616Pts (65%)
Sponsor AstraZeneca

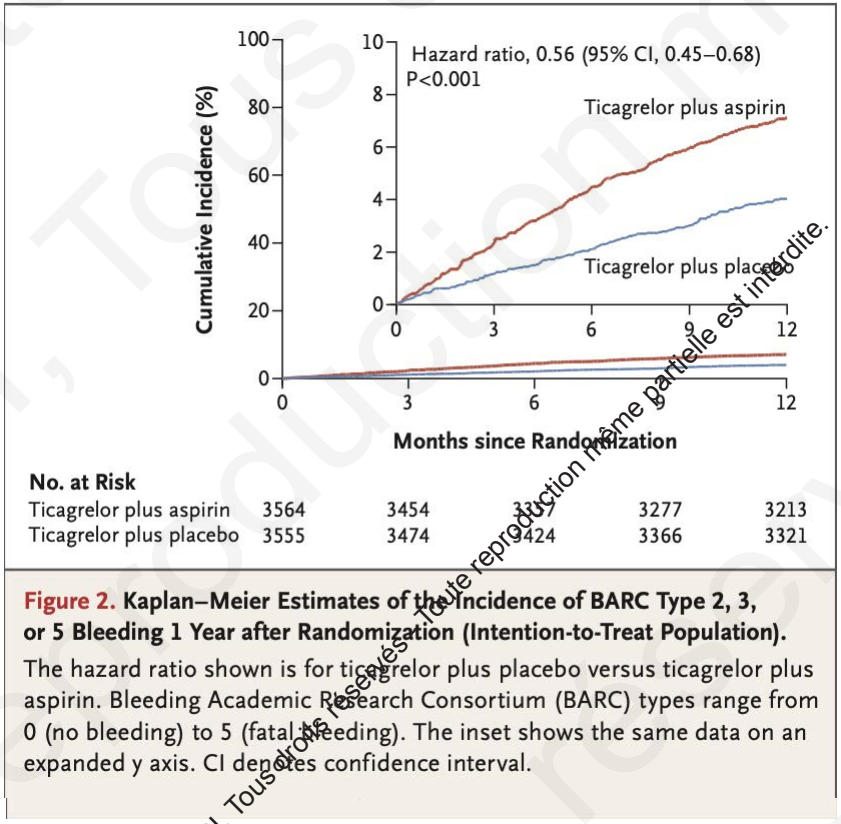
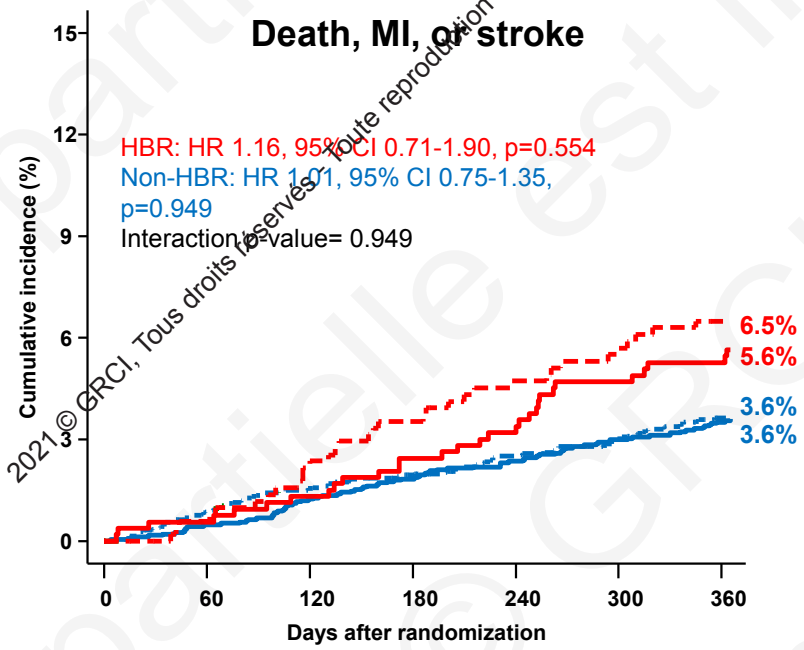


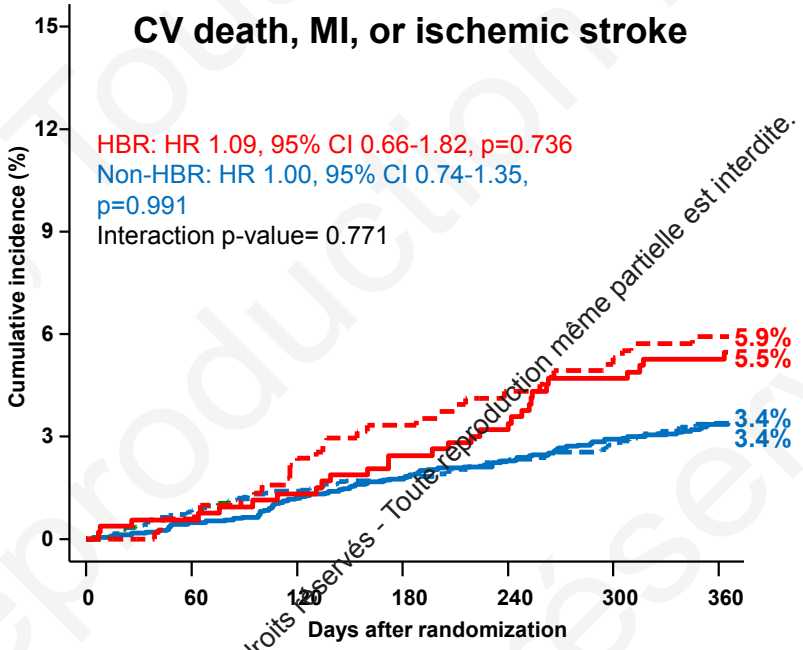
Figure 2. Kaplan–Meier Estimates of the Incidence of BARC Type 2, 3, or 5 Bleeding 1 Year after Randomization (Intention-to-Treat Population).

The hazard ratio shown is for ticagrelor plus placebo versus ticagrelor plus aspirin. Bleeding Academic Research Consortium (BARC) types range from 0 (no bleeding) to 5 (fatal bleeding). The inset shows the same data on an expanded y axis. CI denotes confidence interval.

TWILIGHT-HBR: Ischemic events

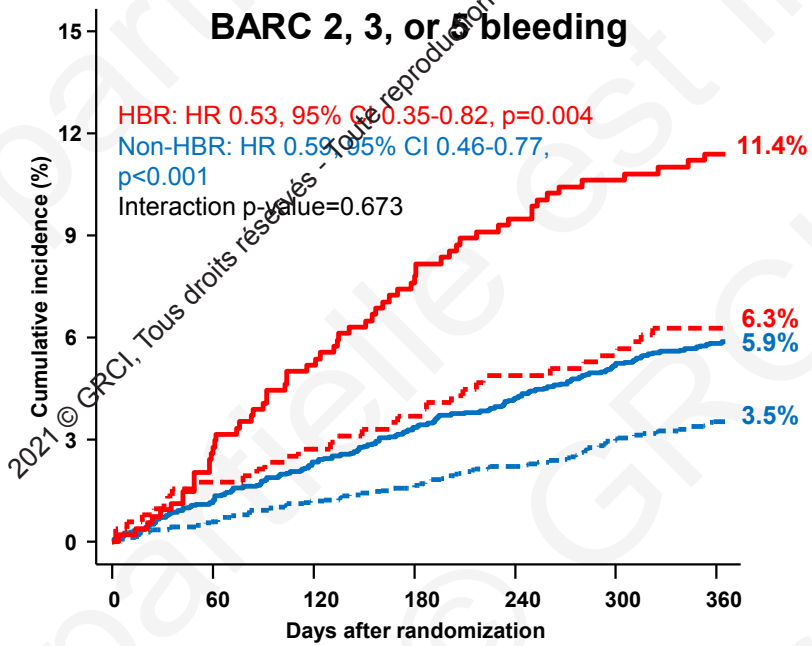
By HBR status & treatment arm

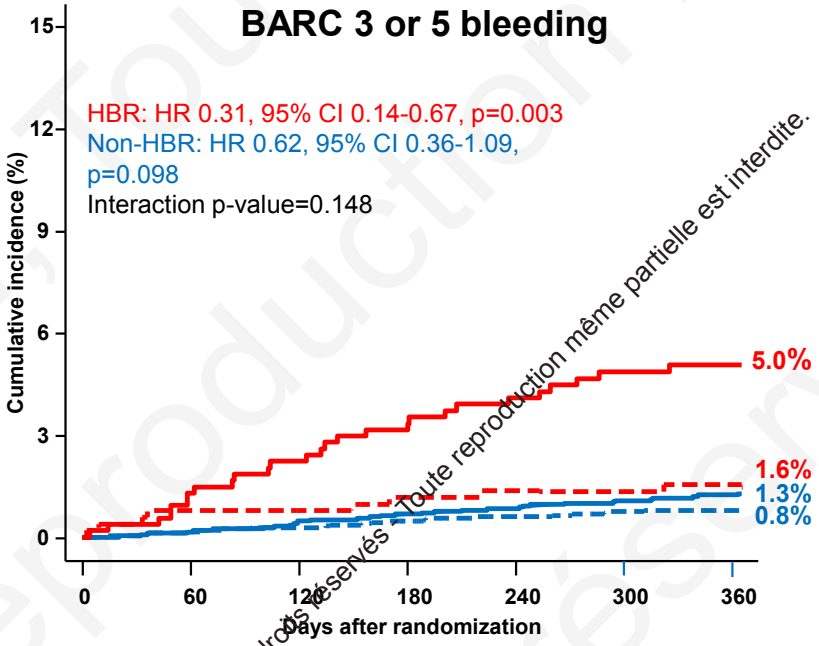




TWILIGHT-HBR: Bleeding

By HBR status & treatment arm



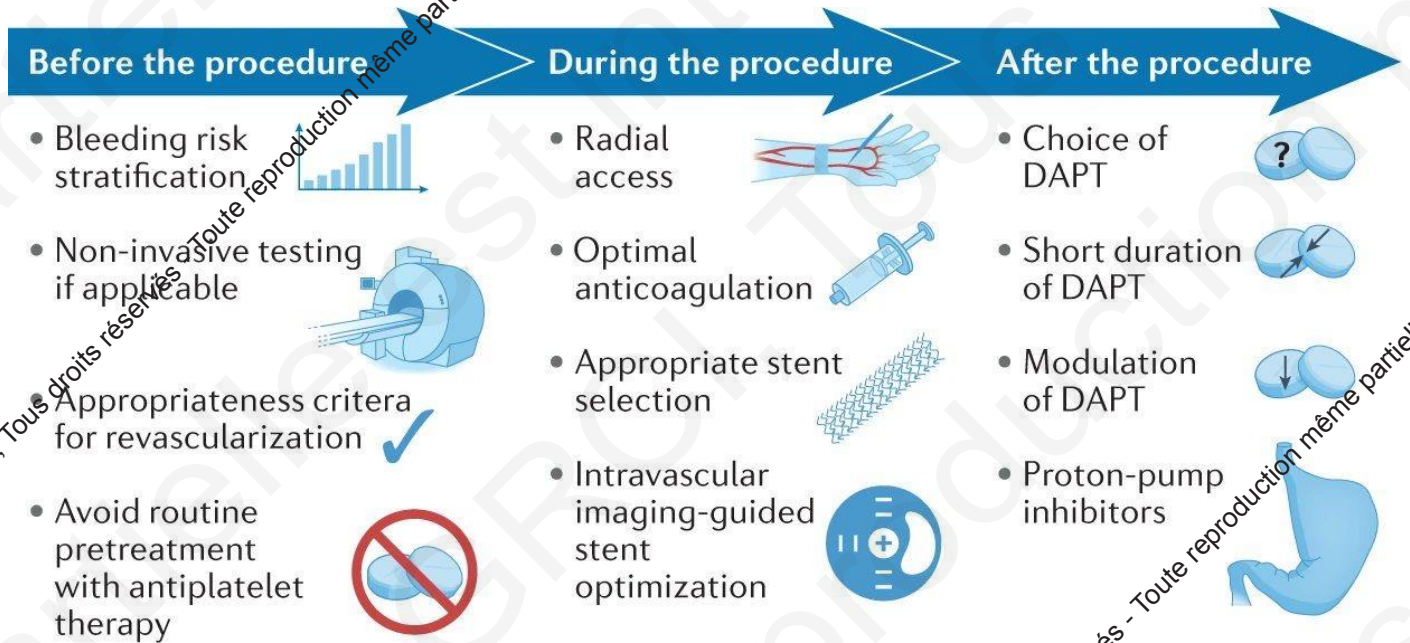


HBR: Tica+Aspirin
HBR: Tica+Placebo
Non-HBR: Tica+Aspirin
Non-HBR: Tica+Placebo

Don’t be afraid of HBR patients
But be afraid if you don’t consider bleeding risk!

- Identify HBR patients (ARC-HBR App)
- Consider non invasive testing as a stratification tool
- Respect appropriate criteria for revascularization
- Avoid routine pre-treatment with ATP agents
- Radial access to reduce vascular complications
- Appropriate stent selection
- Optimal PCI result (Intravascular imaging?)
- DAPT: short – choice – modulation

Bleeding avoidance strategies in PCI



Capodanno D, et al. Nat Rev Cardiol. 2021 Aug. doi: 10.1038/s41569-021-00598-1.

2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.

MR INFORM

First-line Stress CMR vs. coronary angio-FFR
Randomised study 918 CCS Pts
1 year FU

- Less revasc: 36 vs 45%
- Less angio: 48 vs 97%
- Similar MACE rates 3.6 vs 3.7%
- Similar angina @1 year

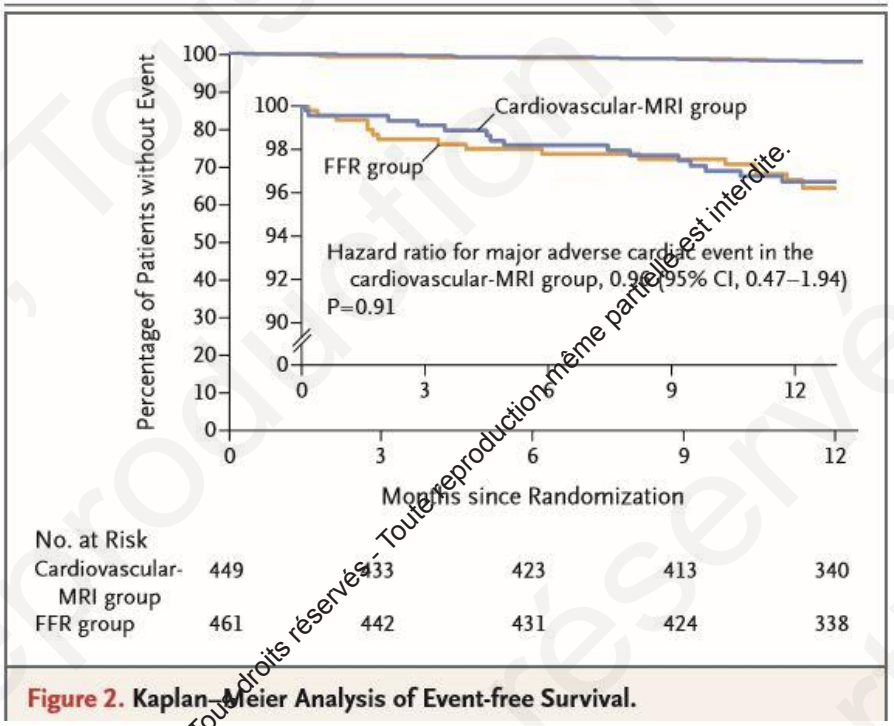
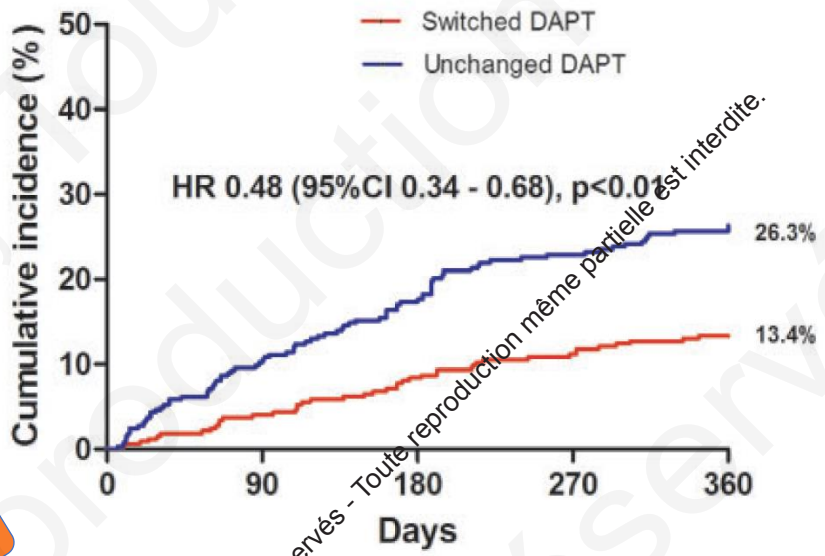


Figure 2. Kaplan–Meier Analysis of Event-free Survival.

Nagel E, et al. N Eng J Med 2019;380:2418-28.

De-escalation: the TOPIC trial

- 645 ACS patients with PCI
- At 30 days, randomly assigned to continue ticagrelor or prasugrel + ASA vs. switch to clopidogrel + ASA
- Primary EP: composite of cardiovascular death, urgent revascularization, stroke and BARC ≥ 2 bleeding
- 1 year FU



No significant differences were reported on ischaemic endpoints, while BARC ≥ 2 bleeding occurred in 13 (4.0%) patients in the switched DAPT and in 48 (14.9%) in the unchanged DAPT group (HR 95%CI 0.30 (0.18–0.50), P < 0.01).

Not HBR patients

Cuisset T et al, EHJ 2017; 38: 3070–3078

Decrease bleeding risk and DAPT duration
How to proceed?

Decrease bleeding risk in HBR Patients - *preventive strategy*

- Individualized antiplatelet treatment regimen
- Short DAPT (1Mo-3Mo)
- DAPT de-escalation - SAPT (P2Y12)
- Early de-escalated DAPT in anticoagulated patients

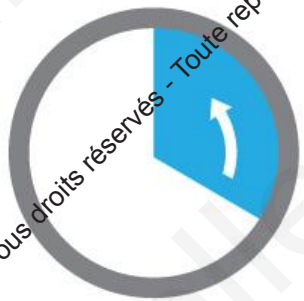
After bleeding: *prevention of reccurrence*

- DAPT shortening, DAPT de-escalation
- SAPT (P2Y12)
- De-escalated DAPT in anticoagulated patients

2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.
2021 © GRCI, Tous droits réservés - Toute reproduction même partielle est interdite.

Tailoring pharmacotherapy for HBR patients

Strategies to reduce the risk of bleeding after PCI



Shortening DAPT

11 TRIALS OF SHORT VS. STANDARD DAPT

De-escalation

TOPIC
TROPICAL ACS

Aspirin withdrawal

GLOBAL LEADERS
SMART-CHOICE
STOPDAPT-2
TWILIGHT

AF + PCI
WOEST
PIONEER- AF-PCI
RE-DUAL PCI
AUGUSTUS
ENTRUST

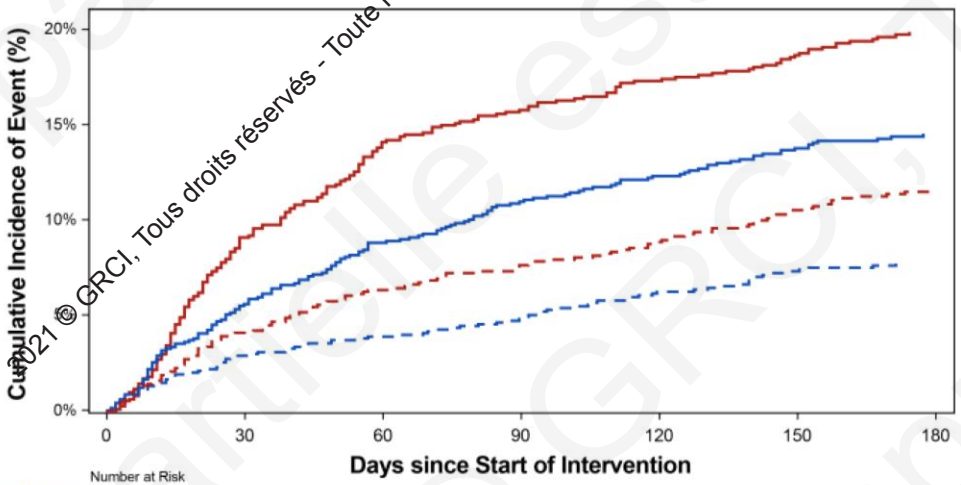
Not HBR patients

Modified from D. Angiolillo

AUGUSTUS trial

- 4614 AF patients with ACS and/or recent PCI
- 2x2 factorial design
  - Apixaban vs VKA & ASA vs placebo
  - **96% on clopidogrel**
- Primary EP: major/clinically relevant bleeding
- 6 months FU

Major/clinically relevant bleeding (ISTH)



Number at Risk

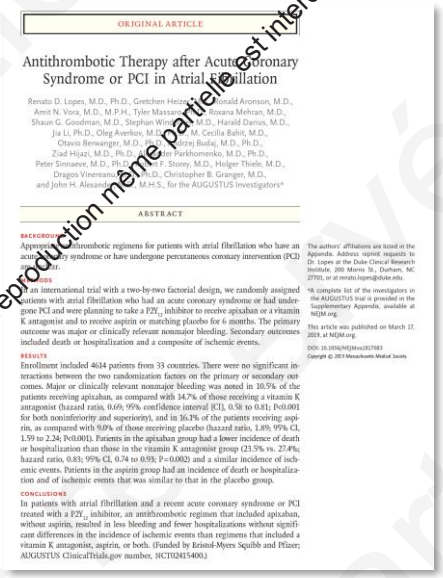
Apixaban and Aspirin	1145	1036	975	937	903	880	485
Apixaban and Placebo	1143	1075	1044	1007	975	947	536
VKA and Aspirin	1123	962	881	838	800	776	467
VKA and Placebo	1126	1007	947	917	883	851	528

VKA + Aspirin (18.7%)

Apixaban + Aspirin (13.8%)

VKA + Placebo (10.9%)

Apixaban + Placebo (7.3%)



ORIGINAL ARTICLE

Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation

ABSTRACT

Lopes RD et al. NEJM 2019

Stents for HBR patients: what we know today

1 month DAPT	BioFreedom (BA9-DCS) Endeavor (ZES)	Significantly better than BMS for both safety (cardiac death or MI) and for efficacy (TLR)
1 or 6 months DAPT	Synergy (EES)	Significantly better than BMS for MACE* *composite of all-cause mortality, MI, stroke, or TLR
1 month DAPT	Onyx (ZES)	Non-inferior to BioFreedom DCS

BMS should no longer be used except for economic reasons

Recent ESC Guidelines for LAAC

2012

Recommendations for LAA closure/occlusion

Recommendations	Class[a]	Level[b]
Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.	IIb	B
Surgical excision of the LAA may be considered in patients undergoing open heart surgery.	IIb	C

LAA = left atrial appendage.
[a]Class of recommendation.
[b]Level of evidence.
[c]References.

2016

Recommendations for occlusion or exclusion of the left atrial appendage

Recommendations	Class[a]	Level[b]	Ref[c]
After surgical occlusion or exclusion of the LAA, it is recommended to continue anticoagulation in at-risk patients with AF for stroke prevention.	I	B	461, 462
LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment (e.g. those with a previous life-threatening bleed without a reversible cause).	IIb	B	449, 453, 454
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery.	IIb	B	463
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients undergoing thoracoscopic AF surgery.	IIb	B	468

Study Endpoints

The study has 3 primary endpoints to be tested in an hierarchical order:

Net adverse clinical events (NACE): the composite of all-cause death, MI, stroke, and major bleeding defined as BARC type 3 or 5

Major adverse cardiac and cerebral events (MACCE): the composite of all-cause death, MI, and stroke

Major or clinically relevant non-major bleeding (MCB): the composite of BARC type 2, 3 and 5 bleeding

The first two primary endpoints were to be tested on a non-inferiority basis in the per protocol population. If non-inferiority was met for both, the third primary endpoint was to be tested on superiority basis in the Intention to treat population. The main analyses evaluate the occurrence of the primary endpoints between randomization and 335 after index PCI

Procedural Characteristics

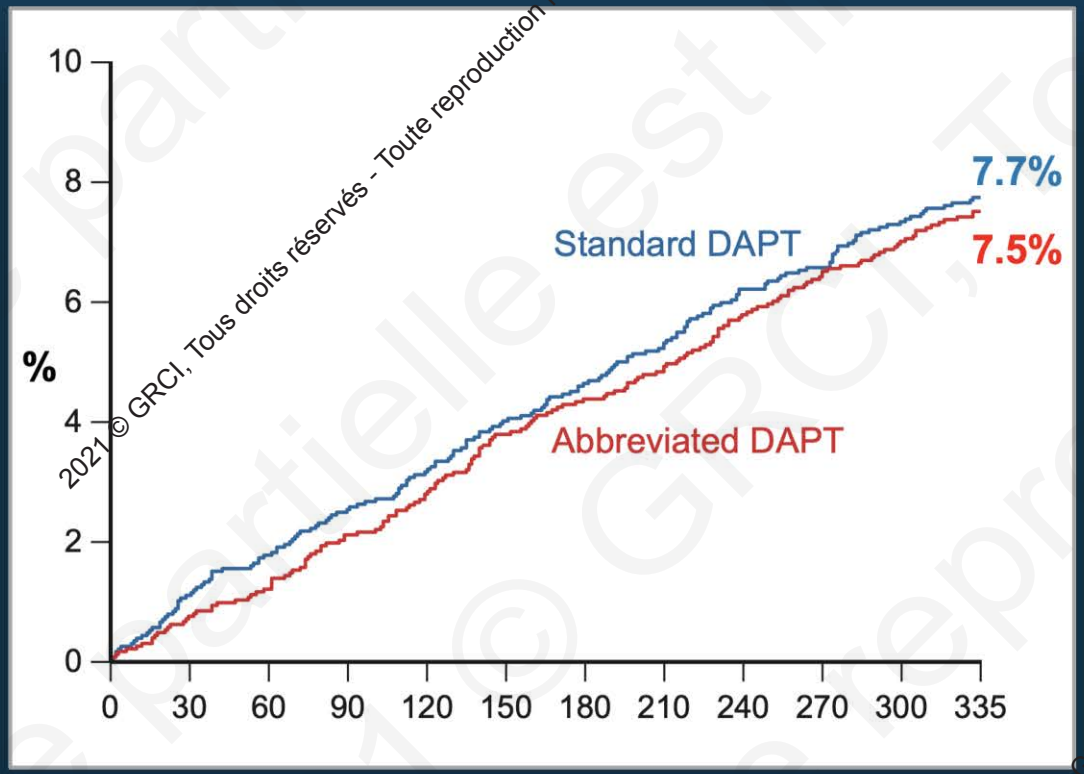
MASTER DAPT

Biodegradable polymer sirolimus-eluting stents were used in 99.8% of the treated lesions in both study groups

	Abbreviated DAPT (N=2295)	Standard DAPT (N=2284)
Arterial access site		
Femoral	360 (15.7)	293 (12.8)
Radial	1930 (84.1)	1984 (86.9)
Multivessel Intervention — no. (%)	579 (25.2)	635 (27.8)
Treated vessel(s) — no. (%)		
Left main	126 (5.5)	134 (5.9)
Left anterior descending artery	1240 (54.0)	1271 (55.6)
Left circumflex artery	652 (28.4)	689 (30.2)
Right coronary artery	854 (37.2)	806 (35.3)
Bypass graft	38 (1.7)	38 (1.7)
≥ one complex lesion B2 or C — no. (%)	1562 (68.1)	1579 (69.1)
Number of stents per patient	1.74±1.13	1.76±1.11
Total stent length per patient	39.3±29.2	39.7±28.4
Overlapping stenting — no. (%)	488 (21.3)	450 (19.7)
Bifurcation/trifurcation stenting — no. (%)	83 (3.6)	101 (4.4)

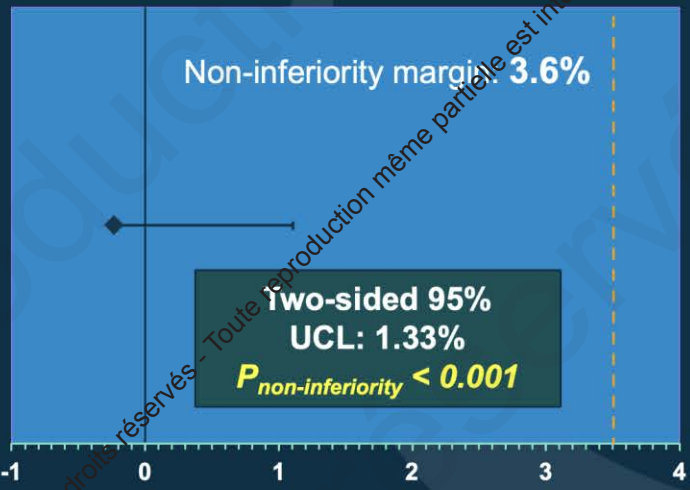
Net adverse clinical events (NACE)

Per protocol population



Non-inferiority Analysis

Difference in cumulative incidence, -0.23



NACE: *All-cause death, MI, stroke, and major bleeding events defined as BARC 3 or 5*