Bithérapie antiplaquettaire : pas si simple!

Guillaume CAYLA
CHU de Nîmes

G Cayla has received research grants/consultant fees/lectures fees from Amgen, AstraZeneca, Abbott, Bayer, Biotronik, Bristol-Myers Squibb, Microport, Medtronic, Pfizer, Sanofi-Aventis.

Durée de la bithérapie antiplaquettaire

PCI

Chronic coronary syndrome

DAPT **6 month**

Acute coronary syndrome

DAPT **12 month**

Bleeding risk

Ischemic risk

Différentes options possibles

Bleeding risk

Ischemic risk

DAPT raccourcie

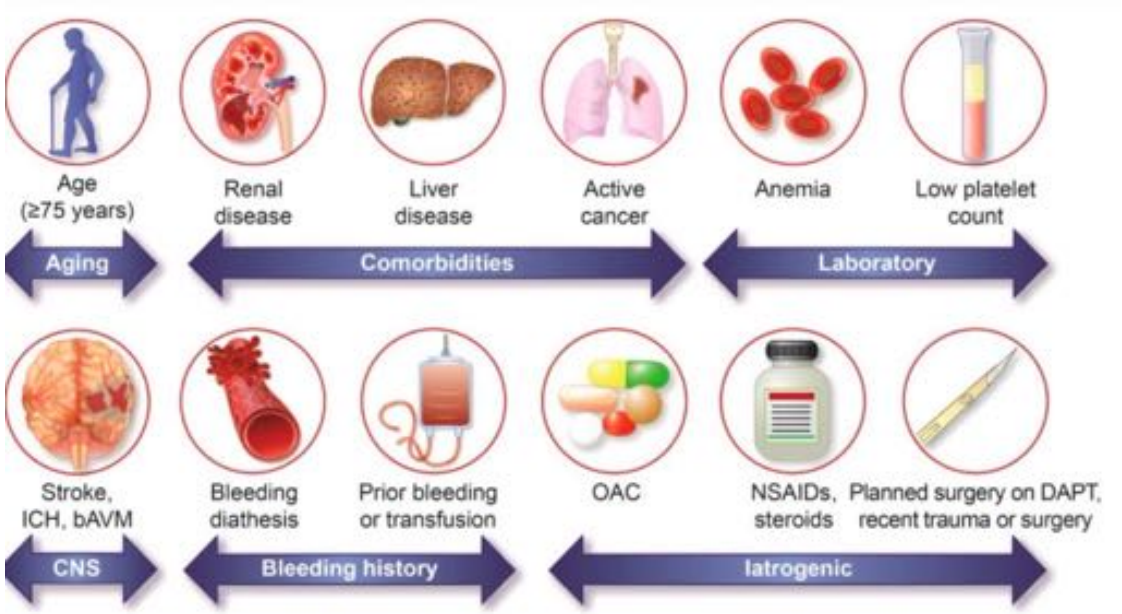
DAPT rallongée

DAPT modifiée

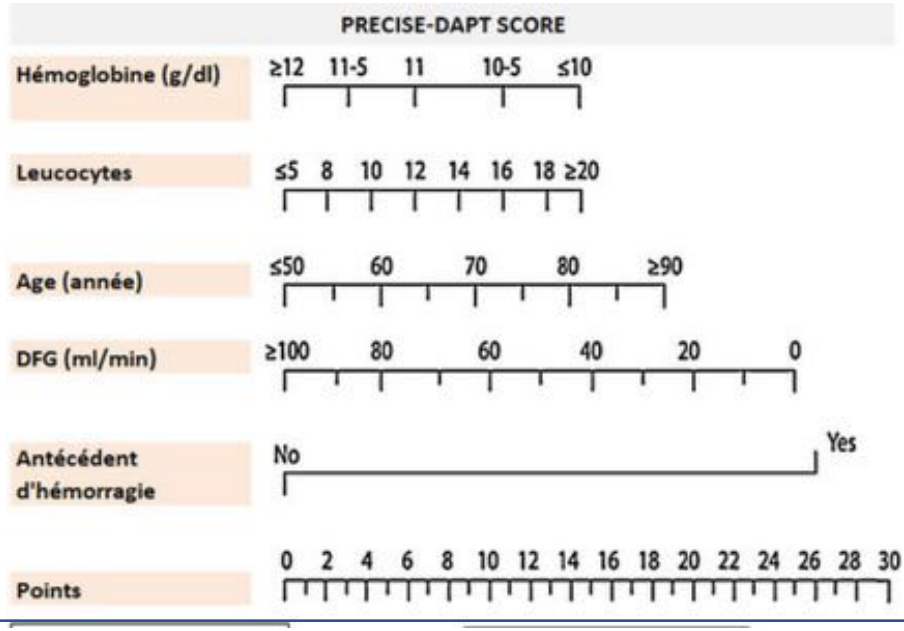
DAPT raccourcie

Risque hémorragique > risque ischémique

HBR patients



Score PRECISE DAPT > 25



DAPT for 1 month DES vs BMS

HBR patients

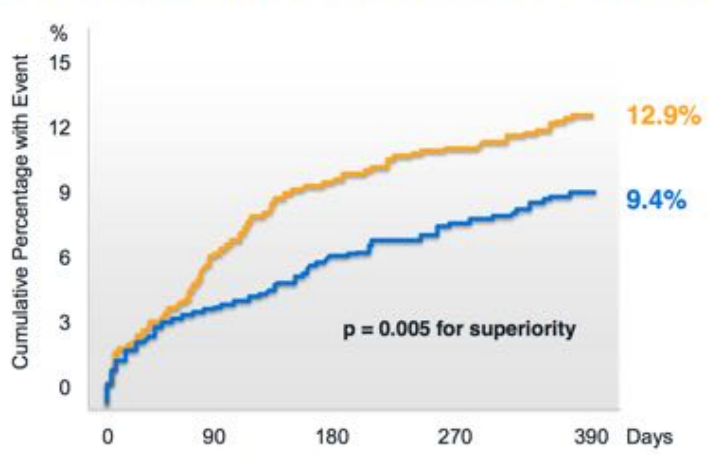
No Randomisation of 2 durations

Comparison of DES *vs* BMS in high risk of bleeding patients using one month DAPT

LEADERS FREE

BIOFREEDOM Stent > BMS

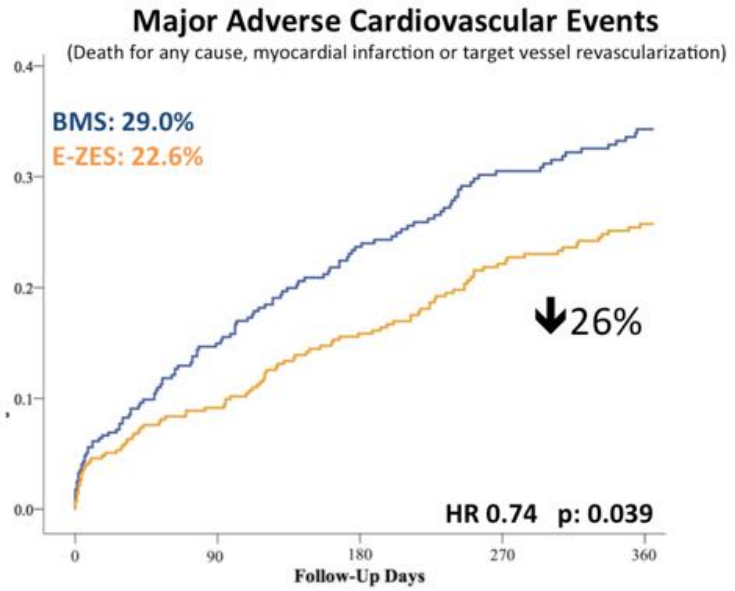
Cardiac Death, MI, ST



Urban P *et al* NEJM 2015

ZEUS

ZOTAROLIMUS Eluting endeavor > BMS

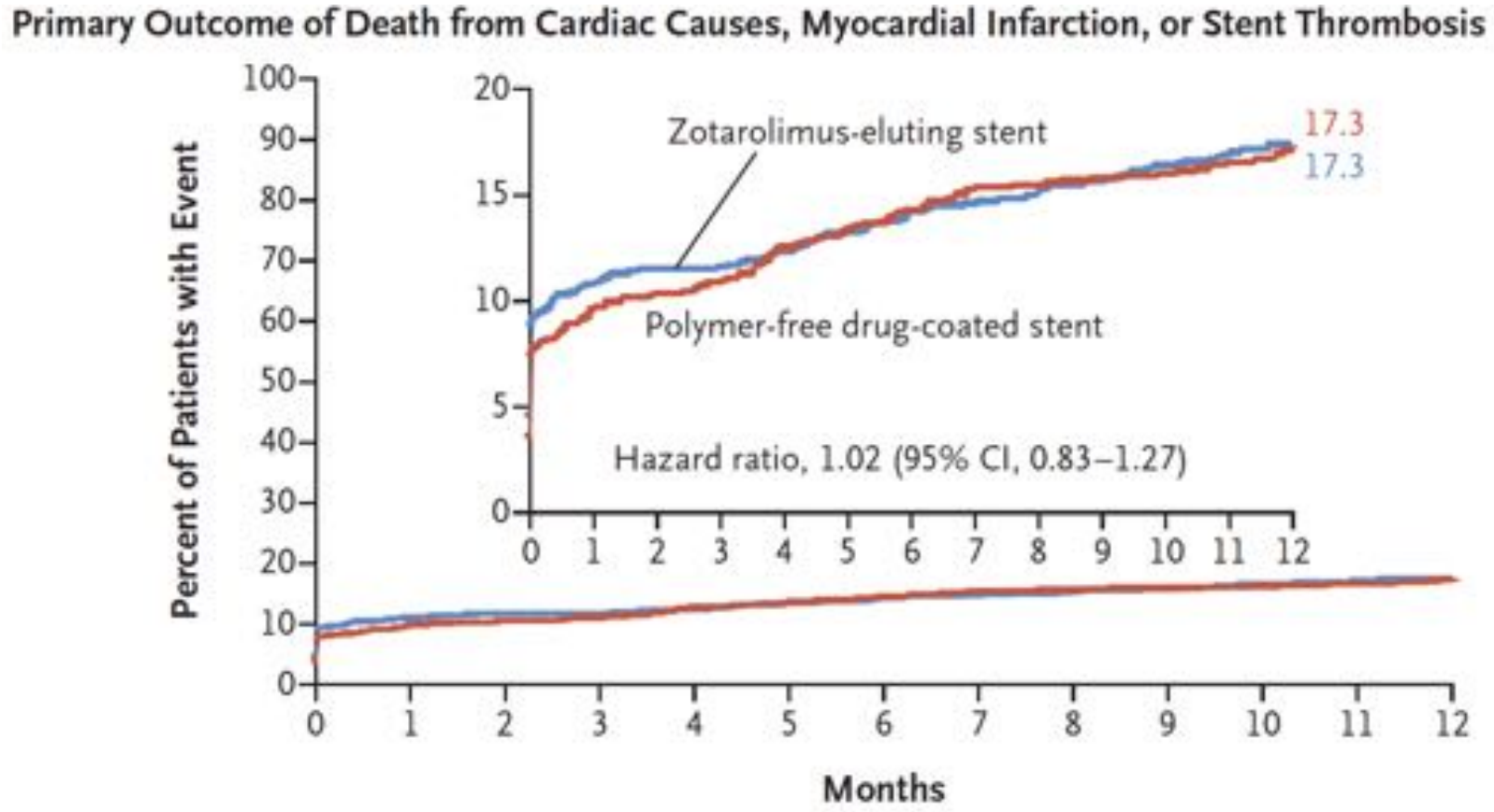


Arrioti S *et al* JACC interv 2016

ONYX ONE

Resolute Onyx™ ZES with 1 Month DAPT (N=1000)	BioFreedom™ DCS with 1 Month DAPT (N=1000)

Mean age 74 y, HBR patients, ACS 50%, n=1996 patients



Marge Non inferiorité 4.1%

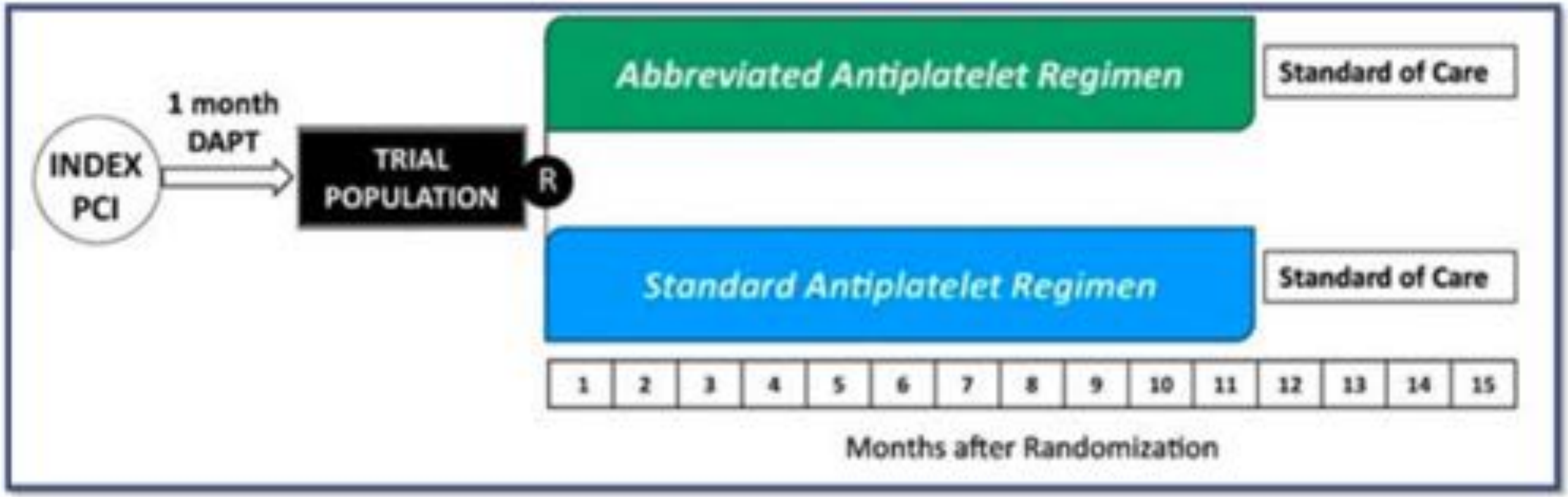
S. Windecker et al NEJM 2020

MASTER DAPT

N=4579 – HBR patients

36% d'OAC

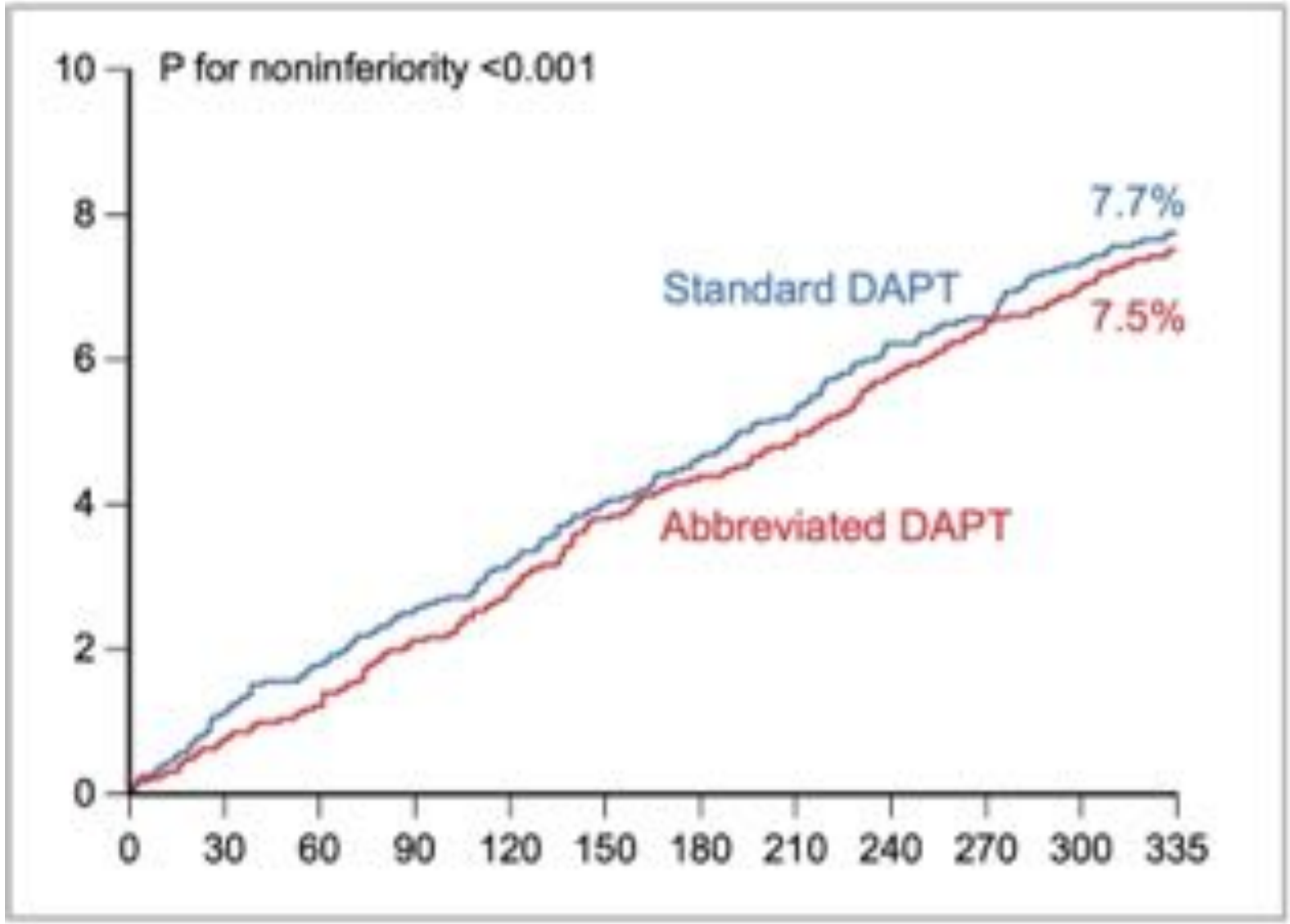
1 mois vs 3 à 12 mois



Randomisation APRES le 1er mois de DAPT

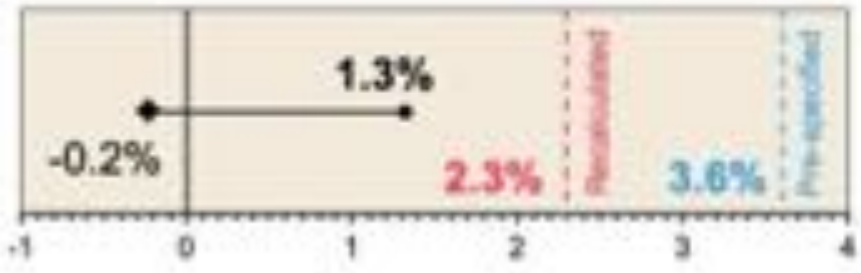
Valgimigli et al NEJM 2021

Résultats principaux

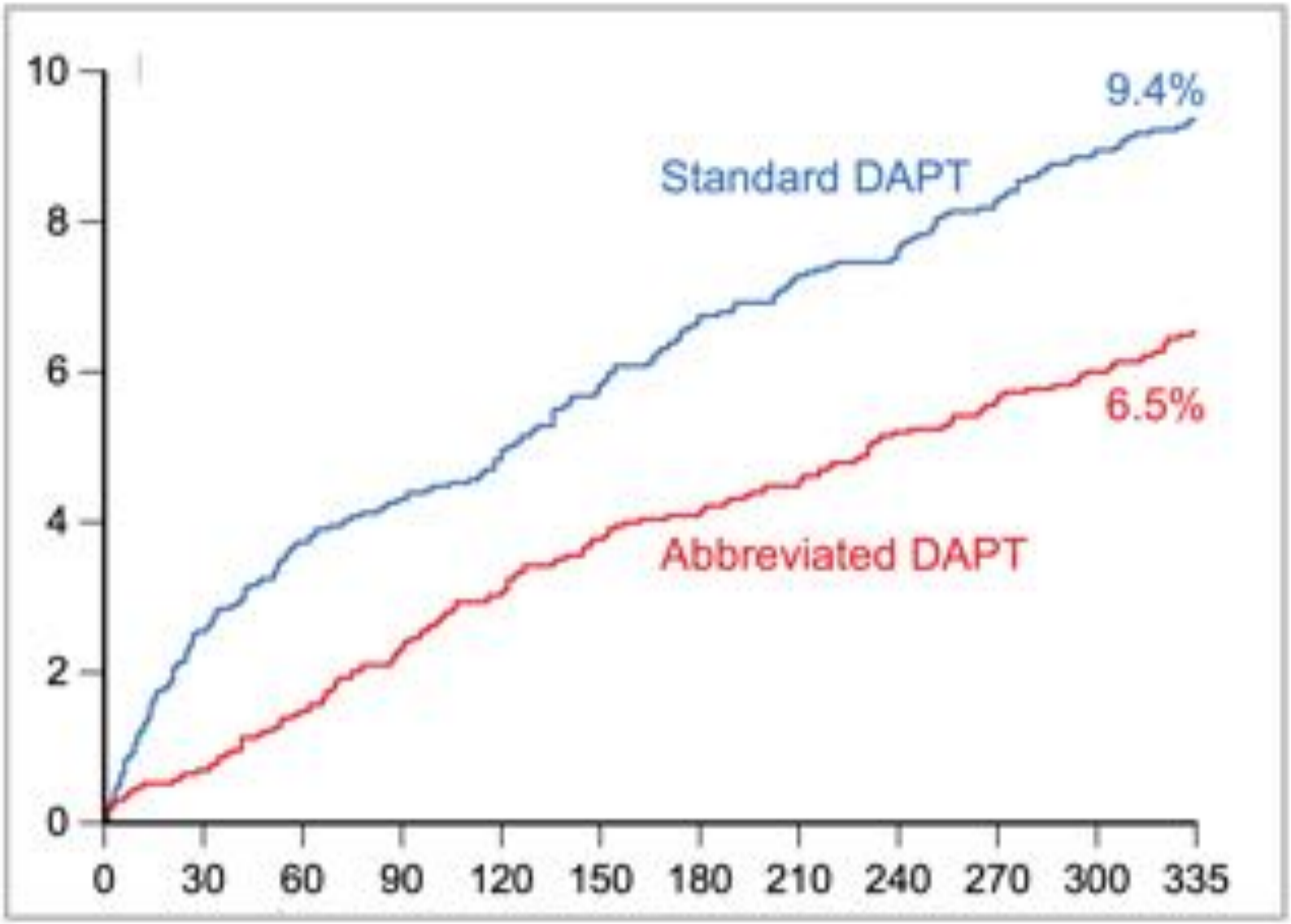


Décès toute cause + IDM + AVC + saignements majeurs (BARC 3/5)

P<0.001
(non infériorité)



Résultats principaux



Saignements cliniquement pertinents et majeurs (BARC 2/3/5)

P<0.001
(supériorité)

Etude randomisée de comparaison de DES chez les patients HBR

Nombre de centres en France: 9/52
Nombre de patients inclus en France : 418/1948

Expected in 2023

BIOFLOW DAPT
N=1,948

BP-SES
Orsiro™

VS

DP-ZES
Resolute Onyx™

Primary endpoint
Death, MI or ST
12 months

NCT04500912, NCT04137510

En pratique PCI High Bleeding risk

3 mois

Shortening antithrombotic treatment duration		
After stent implantation with high risk of bleeding (e.g. PRECISE-DAPT ≥25 or ARC-HBR criteria met), discontinuation of $P2Y_{12}$ receptor inhibitor therapy after 3 months should be considered.[154,226]	IIa	B

1 mois

In patients at very high risk of bleeding, defined as a recent bleeding episode in the past month or planned, not deferrable surgery in the near , 1 month of DAPT should be considered

Collet *et al* ESC guidelines NSTEMI 2020

Plusieurs options possibles

Bleeding risk

Ischemic risk

DAPT raccourcie

DAPT rallongée

DAPT modifiée

Ajout d'un second agent antithrombotique pour la prévention secondaire

Prolonging antithrombotic treatment duration		
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention should be considered in patients with a high risk of ischaemic events and without increased risk of major or life-threatening bleeding (see *Tables 9 and 11* for options).[162,212,213,214,223]	IIa	A

+ Bas risque hémorragique

High thrombotic risk (Class IIa)
Complex CAD and at least 1 criterion
Risk enhancers
Diabetes mellitus requiring medication
History of recurrent MI
Any multivessel CAD
Polyvascular disease (CAD plus PAD)
Premature (<45 years) or accelerated (new lesion within a 2-year time frame) CAD
Concomitant systemic inflammatory disease (e.g. human immunodeficiency virus, systemic lupus erythematosus, chronic arthritis)
CKD with eGFR 15–59 mL/min/1.73 m^2
Technical aspects
At least 3 stents implanted
At least 3 lesions treated
Total stent length >60 mm
History of complex revascularization (left main, bifurcation stenting with ≥2 stents implanted, chronic total occlusion, stenting of last patent vessel)
History of stent thrombosis on antiplatelet treatment

Collet *et al* ESC guidelines NSTEMI 2020

Ajout d'un second agent antithrombotique pour la prévention secondaire

Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention may be considered in patients with moderately increased risk of ischaemic events and without increased risk of major or life-threatening bleeding (see *Tables 9 and 11* for options).[162,212,213,214,223]	IIb	A

+

Bas risque hémorragique

Moderate thrombotic risk (Class IIb)
Non-complex CAD and at least 1 criterion
Diabetes mellitus requiring medication
History of recurrent MI
Polyvascular disease (CAD plus PAD)
CKD with eGFR 15–59 mL/min/1.73 m^2

Collet *et al* ESC guidelines NSTEMI 2020

DAPT rallongée: quelles options?

Drug	Dose	Indication	NNT (ischaemic outcomes)	NNH (bleeding outcomes)
DAT regimens for extended treatment (including aspirin 75–100 mg o.d.)				
Rivaroxaban (COMPASS trial)	2.5 mg b.i.d.	Patients with CAD or symptomatic PAD at high risk of ischaemic events	77	84
DAPT regimens for extended treatment (including aspirin 75–100 mg o.d.)				
Clopidogrel (DAPT trial)	75 mg/d	Post MI in patients who have tolerated DAPT for 1 year	63	105
Prasugrel (DAPT trial)	10 mg/d (5 mg/d if body weight <60 kg or age >75 years)	Post PCI for MI in patients who have tolerated DAPT for 1 year	63	105
Ticagrelor (PEGASUS-TIMI 54)	60/90 mg b.i.d.	Post MI in patients who have tolerated DAPT for 1 year	84	81

Collet *et al* ESC guidelines NSTEMI 2020

Plusieurs options possibles

Bleeding risk

Ischemic risk

DAPT raccourcie

DAPT rallongée

DAPT modifiée

De escalade : **intense $P2Y_{12}$ inhibiteur** → **Clopidogrel**

De-escalade prévue

prevention des effets secondaires

améliorer l'adherence au traitement

De-escalade non prévue

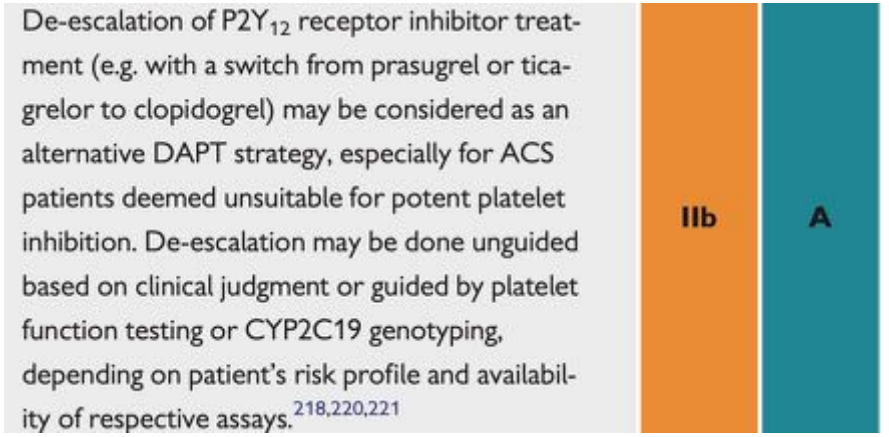
En reaction aux effets secondaires

De escalade

Basée sur le jugement clinique: TOPIC

Basée sur test biologique génotypique CYP 2C19 ou test fonctionnel plaquettaire

TROPICAL- POPULAR GENETIC



Collet *et al* ESC guidelines NSTEMI 2020

Monothérapie par inhibiteur P2Y12

Bithérapie initiale (1 à 6 mois) puis monothérapie par inhibiteur P2Y12

stop aspirine, **$P2Y_{12}$ monotherapy**

- Clopidogrel after 1 month (STOP DAPT 2/ STOP DAPT ACS)
- Ticagrelor after 1-3 months (GLOBAL LEADERS/TWILIGHT/TICO)

Pourquoi garder inhibiteur P2Y12 seul?

Pour

Effet spécifique sur thrombose de stent

Pas d'effet indésirables gastro intestinaux

Pas de résistant biologique avec prasugrel ou ticagrelor

Contre

Resistant biologique au clopidogrel

Les études récentes

	STOP DAPT 2 STOP DAPT ACS	SMART CHOICE	TWILIGHT	TICO
Durée DAPT	1 mois	3 mois	3 mois	3 mois
Aprés DAPT	Clopi/prasu (1/3)	Clopidogrel/tica (1/5)	100% ticagrelor	100% ticagrelor
%ACS T+	24.5% 100%	25.4%	30.8%	71.1%

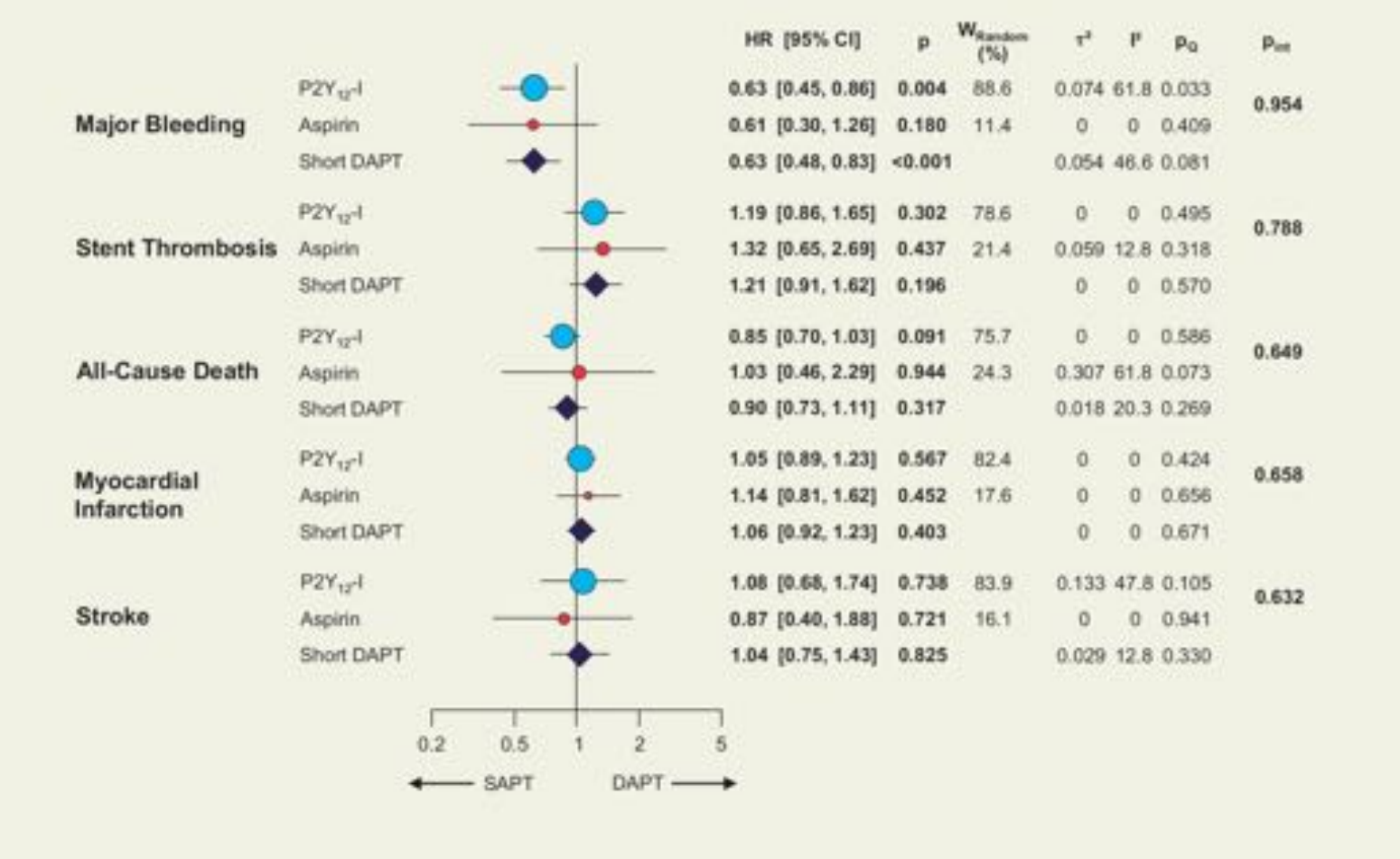
Meta analyse short DAPT 1-3 mois

Arrêt Aspirine

Arrêt Clopidogrel

GLOBAL LEADERS, SMART CHOICE, STOP DAPT 2, TWILIGHT TICO N=32 145 patients

RESET, OPTIMIZE, REDUCE



Giacoppo et al EHJ 2020

Monothérapie par inhibiteur P2Y12

Bithérapie initiale puis monothérapie par inhibiteur P2Y12

stop aspirine, $P2Y_{12}$ monotherapy

After stent implantation in patients undergoing a strategy of DAPT, stopping aspirin after 3–6 months should be considered, depending on the balance between the ischaemic and bleeding risk.[208,209,227]	IIa	A

Collet *et al* ESC guidelines NSTEMI 2020

TARGET FIRST

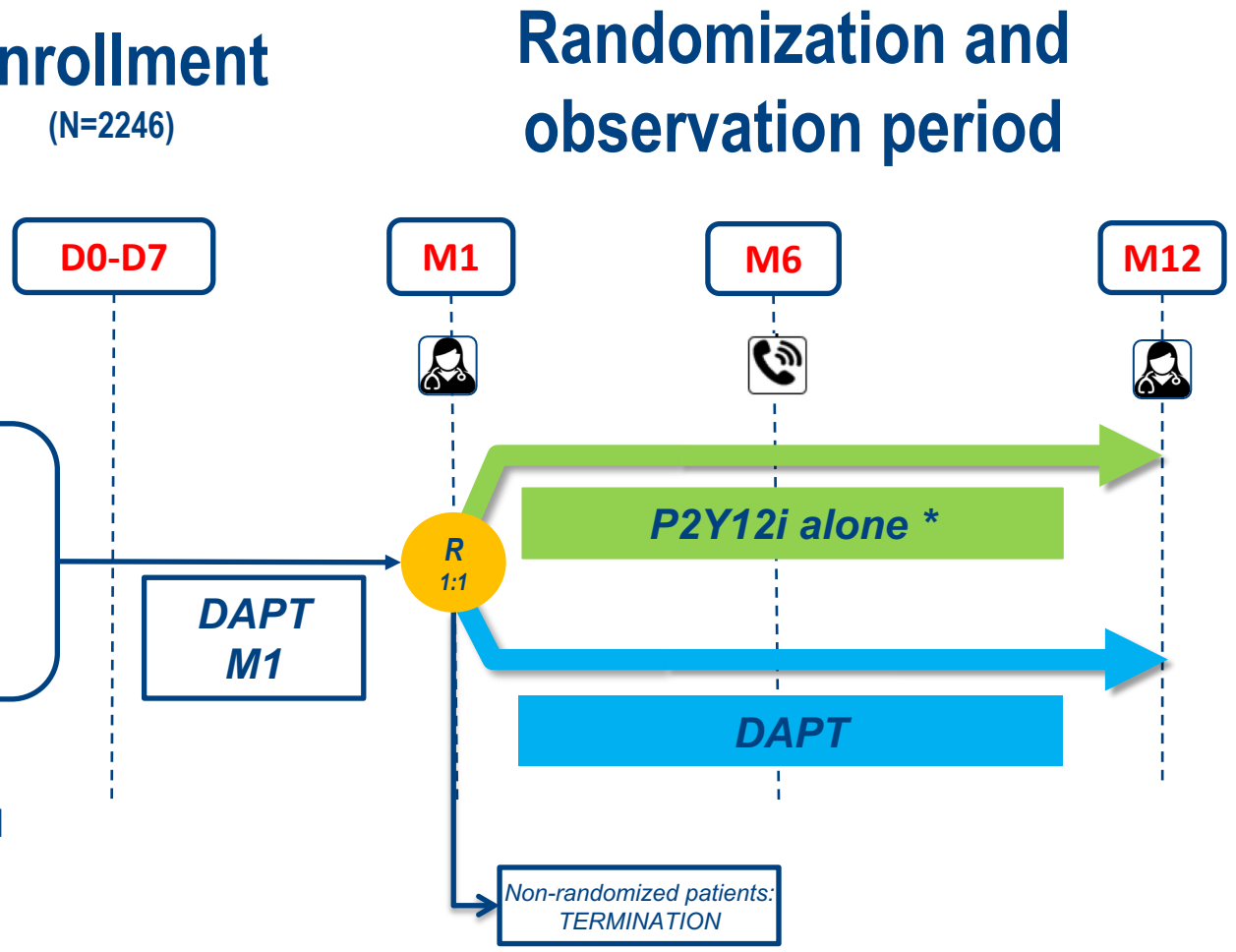
6 pays, 37 centres (18 centres français)

N=2246 Patients

+ de 600 patients inclus

FIREHAWK™
Rapamycin Target Eluting Coronary Stent System

NSTEMI & STEMI subjects with successful (complete) revascularization, with Firehawk
and
within 7 days post index procedure



*Primary endpoint (*ITT*):* NACCE composite of all cause death, MI, definite/probable ST , stroke, or BARC 3/5 bleeding – M1 to M12

(*) $P2Y_{12}$ inhibitor selected by investigator at enrollment, based on current ESC guidelines

MicroPort

Conclusion

La durée de la bithérapie est standardisée 12 mois ACS et 6 mois CCS

La durée courte de la bithérapie chez les patients HBR a été très étudiée avec des résultats favorables

Les données concernant la possibilité d'arrêter l'aspirine en poursuivant le P2Y12 I s'accumulent

La stratégie d'inhibiteur P2Y12 sans aspirine semble être une voie d'avenir et pourrait être dans le futur un nouveau standard?