DAPT → Des recommandations à la vraie vie

Hôpital Pitié-Salpêtrière AP-HP

JP Collet for the ACTION group

ACTION Group

Dr. Collet reports research Grants to the Institution or Consulting/Lecture Fees from Abbott, AstraZeneca, Boston Scientific, Bristol-Myers Squibb, Medtronic, Pfizer.

SORBONNE UNIVERSITÉ

16ème Forum Européen

Paris, France

action-groupe.org

DAPT duration in ACS

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

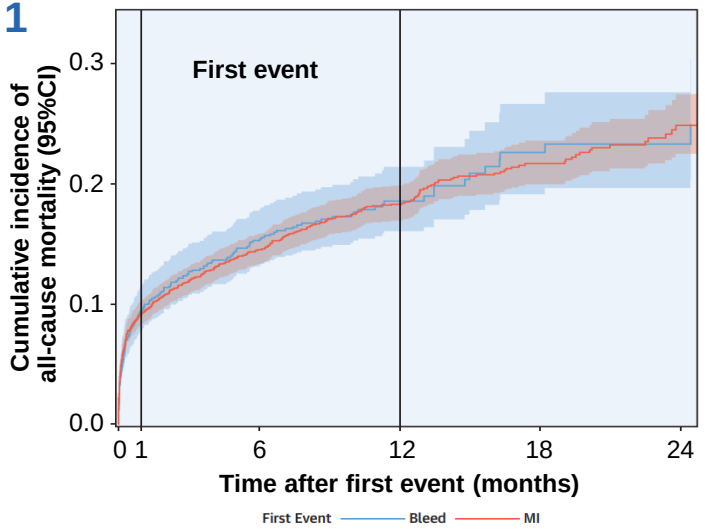
Post-interventional and maintenance treatment	Class	Level
In patients with NSTE-ACS treated with coronary stent implantation, DAPT with a $P2Y_{12}$ receptor inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as excessive risk of bleeding	I	A

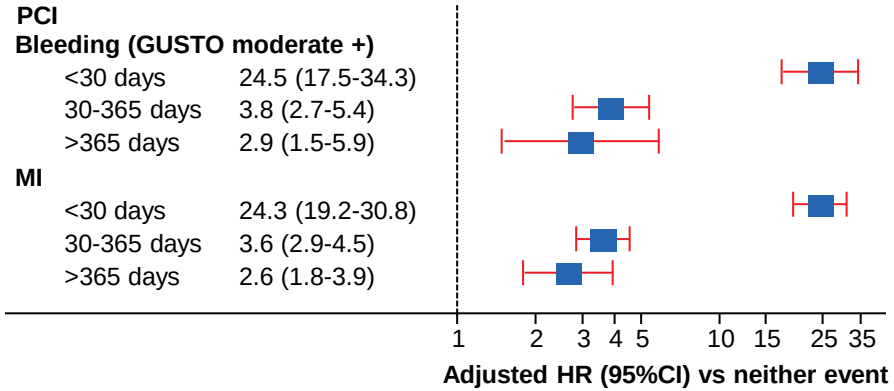
Collet JP, Thiele H, et al. Eur Heart J. 2021;42:1289-1367

Trade-off between MI vs bleeding

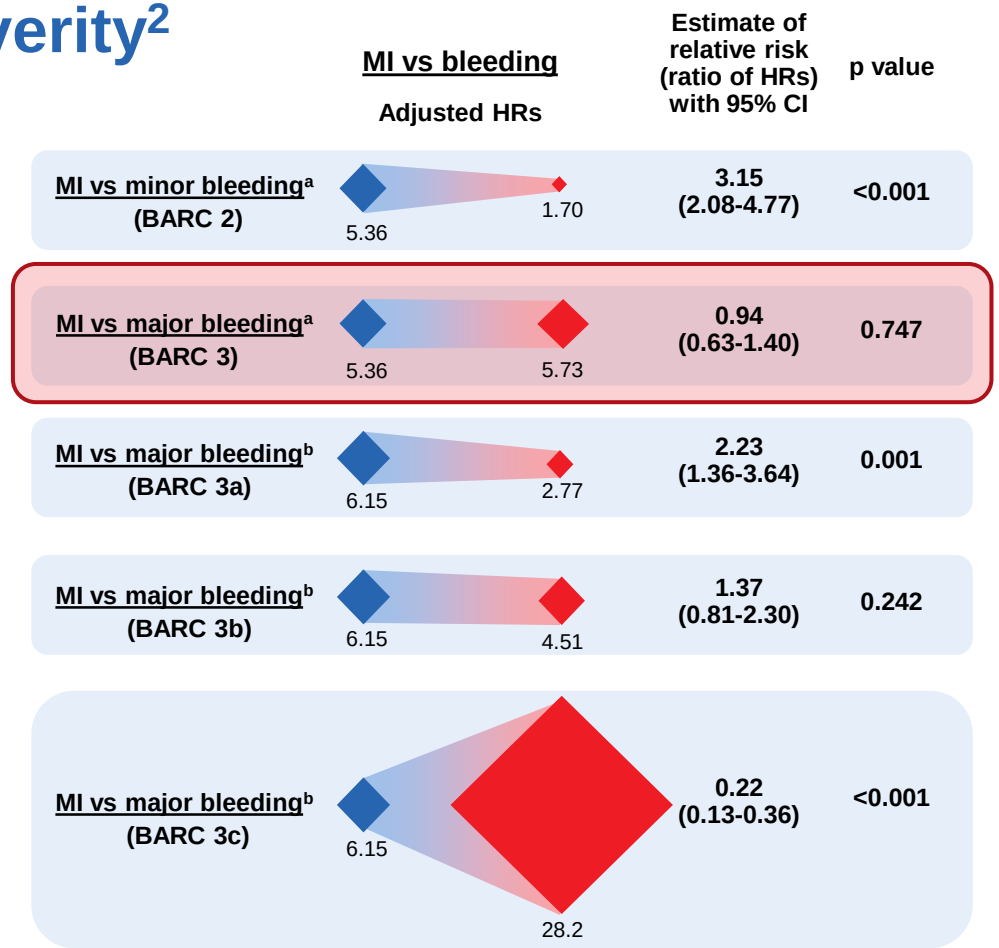
Mortality after MI = mortality after major bleeding

a.) Timing[1]





b.) Severity[2]



BARC, Bleeding Academic Research Consortium grade; CI, confidence interval; GUSTO, global use of strategies to open occluded coronary arteries; HR, hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention

1. Marquis-Gravel G, et al. J Am Coll Cardiol. 2020;76:162-71; 2. Valgimigli M, et al. Eur Heart J. 2017;38:804-10

Should we shorten it?

Academic Research Consortium High Bleeding Risk Criteria

Expected rate of major bleeding (BARC 3 or 5) ≥4% or intracranial bleeding ≥1% at 12 months ➔ 1 major or 2 minor criteria

Major	Minor
	Age ≥75 y
Anticipated use of long-term oral anticoagulation*	
Severe or end-stage CKD (eGFR <30 mL/min)	Moderate CKD (eGFR 30–59 mL/min)
Hemoglobin <11 g/dL	Hemoglobin 11–12.9 g/dL for men and 11–11.9 g/dL for women
Spontaneous bleeding requiring hospitalization or transfusion in the past 6 mo or at any time, if recurrent	Spontaneous bleeding requiring hospitalization or transfusion within the past 12 mo not meeting the major criterion
Moderate or severe baseline thrombocytopenia† (platelet count <100×10⁹/L)	
Chronic bleeding diathesis	
Liver cirrhosis with portal hypertension	
	Long-term use of oral NSAIDs or steroids
Active malignancy‡ (excluding nonmelanoma skin cancer) within the past 12 mo	
Previous spontaneous ICH (at any time) Previous traumatic ICH within the past 12 mo Presence of a bAVM Moderate or severe ischemic stroke§ within the past 6 mo	Any ischemic stroke at any time not meeting the major criterion
Nondeferrable major surgery on DAPT	
Recent major surgery or major trauma within 30 d before PCI	

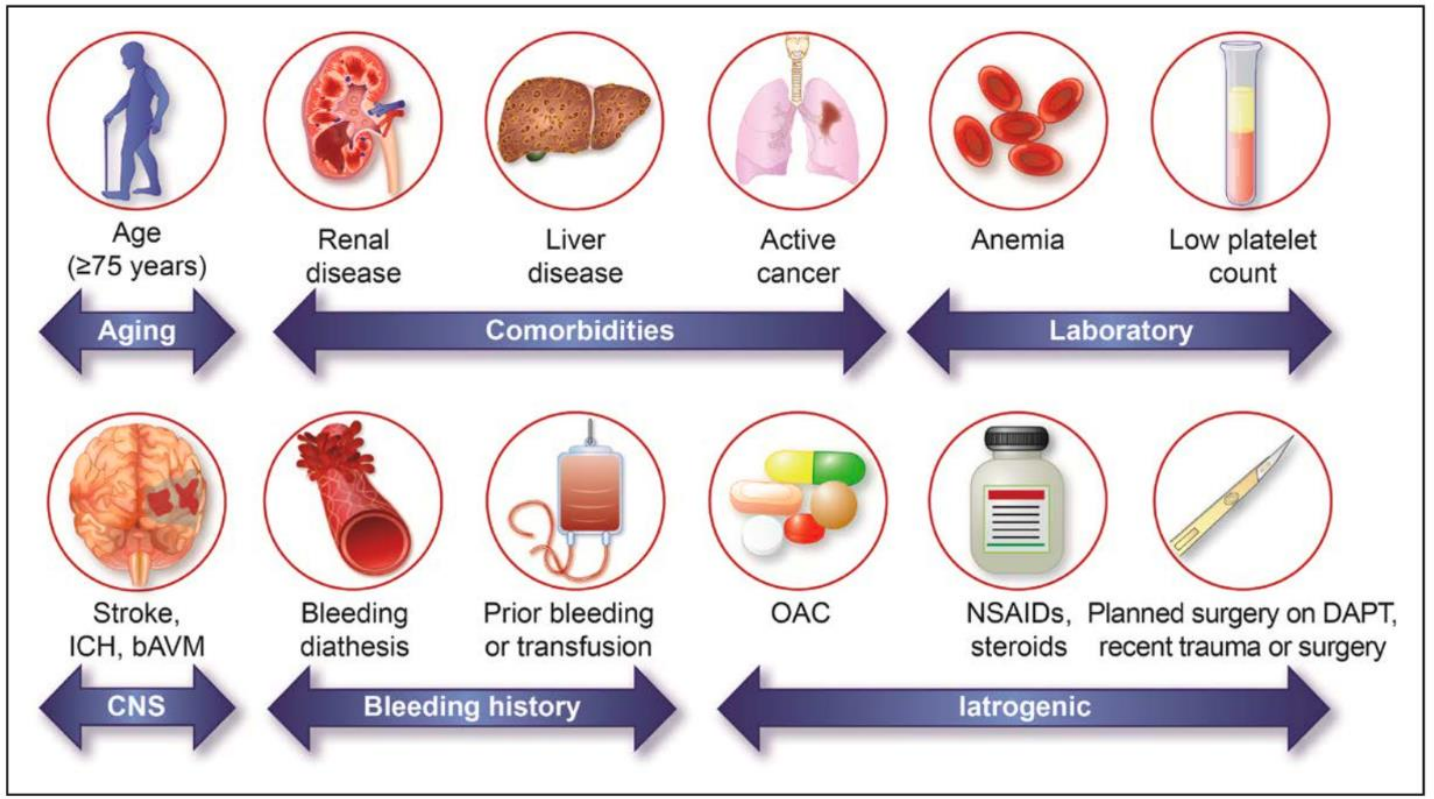


Figure. Factors associated with an increased bleeding risk after percutaneous coronary intervention.
bAVM indicates brain arteriovenous malformation; CNS, central nervous system; DAPT, dual antiplatelet treatment; ICH, intracranial hemorrhage; NSAID, nonsteroidal anti-inflammatory drug; and OAC, oral anticoagulation.

www.escardio.org/guidelines

Urban P et al. Circulation. 2019 Jul 16;140(3):240-261

P2Y12-i discontinuation in ACS

SMART-DATE

MULTICENTER, RANDOMIZED, OPEN-LABEL

2,712 Patients with UA, NSTEMI or STEMI

	Short DAPT ($P2Y_{12}$-i 6-mo)	Standard ($P2Y_{12}$-I 12-mo)
MACE at 18 mo	4.7%	4.2%
	P_{NI}=0.03	
MI	1.8%	0.8%

Short DAPT was NI (but unsafe?)

Lancet 2018;391:1274-1284

REDUCE-ACS

MULTICENTER, RANDOMIZED, OPEN-LABEL

1,496 Patients with UA, NSTEMI or STEMI

	Short DAPT ($P2Y_{12}$-i 3-mo)	Standard $P2Y_{12}$-I 12-mo
NACE at 12 mo	8.2%	8.4%
	P_{NI}<0.001	
ST	1.6%	0.8%

Short DAPT was NI (but unsafe?)

EuroIntervention 2019;15:e990-e998

DAPT-STEMI

MULTICENTER, RANDOMIZED, OPEN-LABEL

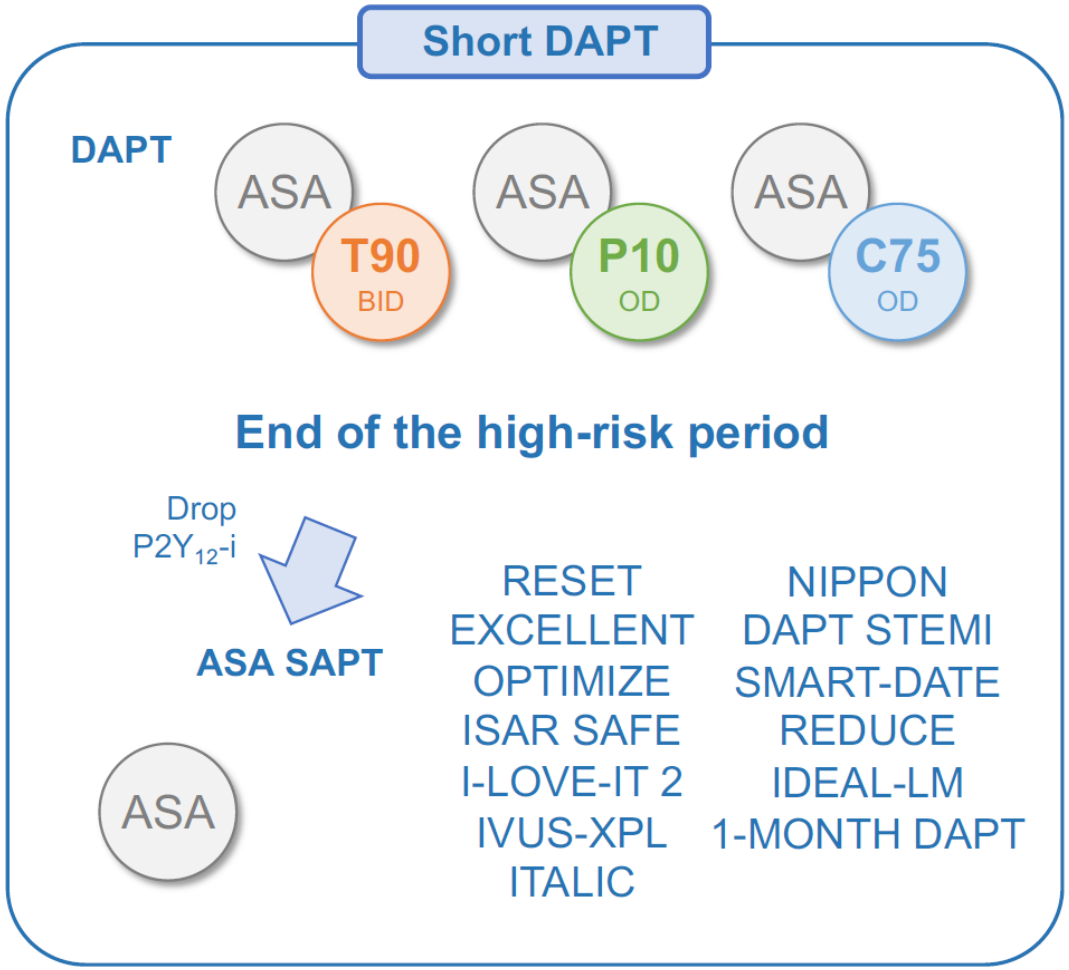
870 Patients with STEMI on DAPT, event-free at 6 mo

	SAPT (aspirin only)	DAPT ($P2Y_{12}$-I 18-mo)
NACE at 18 mo	4.8%	5.5%
	P_{NI}=0.004	
MI	1.8%	1.8%

Short DAPT was NI (large NI margin)

BMJ 2018;363:k3793

Updated metanalysis



Short DAPT (→ASA) vs standard DAPT

NMA (13 trials, N=32,679)	RR (95% CI)
All-cause death	0.93 (0.69 – 1.25)
NACE	1.03 (0.90 – 1.18)
MACE	1.04 (0.87 – 1.24)
Cardiovascular death	0.95 (0.62 – 1.44)
Myocardial infarction	1.20 (0.90 – 1.59)
Stroke	0.90 (0.56 – 1.44)
Stent thrombosis	1.45 (0.93 – 2.27)
Clinically relevant bleeding	0.81 (0.55 – 1.19)
Major bleeding	0.91 (0.49 – 1.71)
Minor bleeding	0.58 (0.17 – 1.99)

Laudani C, Capodanno D, et al. JACC Cardiovasc Interv. 2022;15:268-277

Discontinuation of P2Y12-i

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Post-interventional and maintenance treatment	Class	Level
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.	IIa	B

Collet JP, Thiele H, et al. Eur Heart J. 2021;42:1289-1367

Aspirin discontinuation in ACS

TICO

MULTICENTER, RANDOMIZED, OPEN-LABEL

3,056 ACS patients who underwent PCI at 38 hospitals in South Korea

	Ticagrelor (after 3-mo of DAPT)	DAPT (12-mo)
NACE at 12 mo	3.9%	5.6%
	HR 0.66 (0.48-0.92); P=0.01	
Major bleeding	1.7%	3.0%
	P=0.02	

3-mo DAPT resulted in significantly lower NACE

Kim BK, et al. JAMA. 2020;323:2407-2416

STOPDAPT-2 ACS

MULTICENTER, RANDOMIZED, OPEN-LABEL

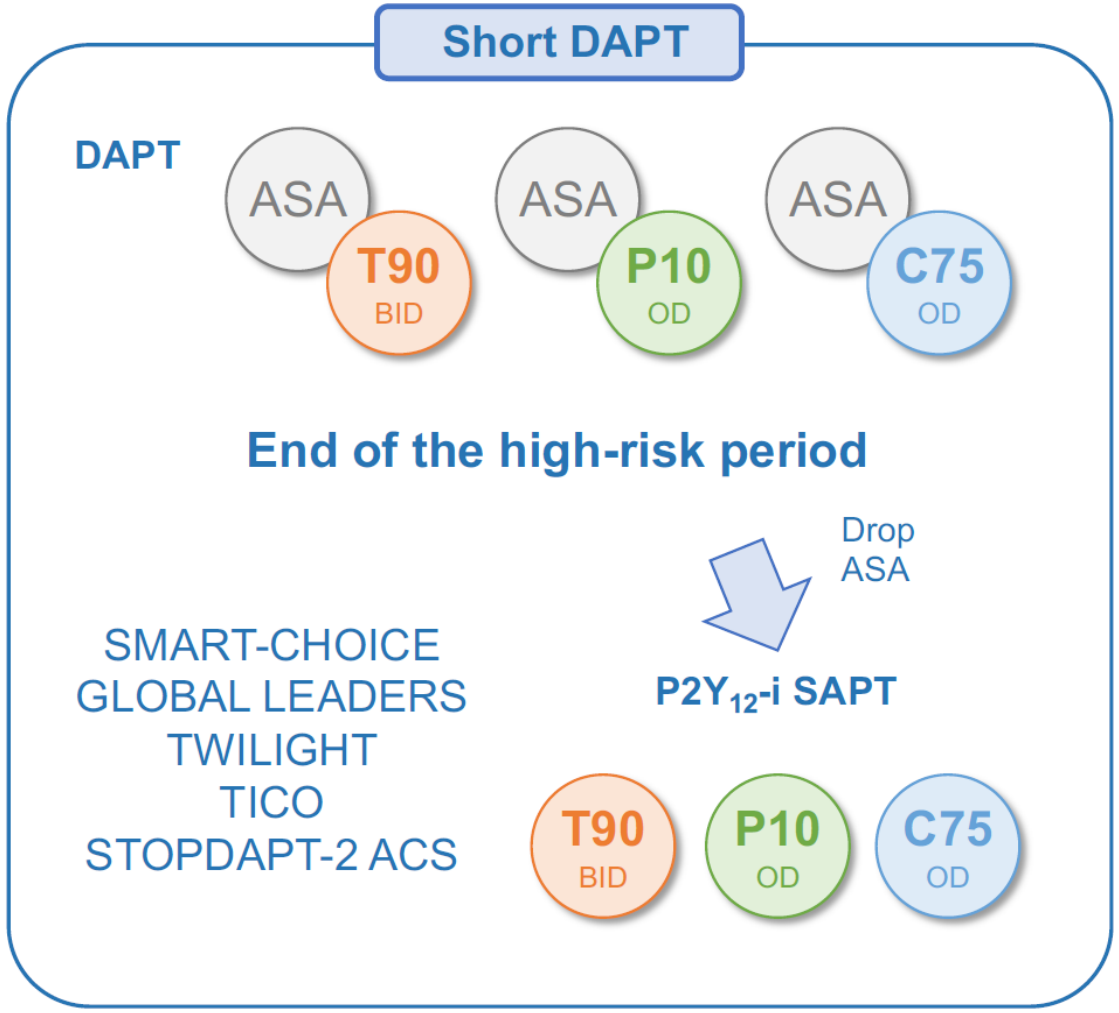
4,169 ACS patients who underwent PCI at 96 hospitals in Japan

	Clopidogrel (after 1/2-mo of DAPT)	DAPT (12-mo)
NACE at 12 mo	3.2%	2.8%
	HR 1.14 (0.80-1.62); P_{NI}=0.06	
Major bleeding	0.5%	1.2%
	P=Sig.	

1-mo DAPT was not noninferior for NACE

Watanabe H. JAMA. 2022;ePub ahead of print

Updated metanalysis



Short DAPT (→P2Y$_{12}$-i) vs standard DAPT

NMA (5 trials, N=35,931)	RR (95% CI)
All-cause death	0.83 (0.66 – 1.05)
NACE	0.85 (0.73 – 0.98)
MACE	0.91 (0.78 – 1.06)
Cardiovascular death	0.58 (0.23 – 1.48)
Myocardial infarction	1.09 (0.90 – 1.33)
Stroke	1.15 (0.80 – 1.66)
Stent thrombosis	1.07 (0.71 – 1.62)
Clinically relevant bleeding	0.59 (0.43 – 0.80)
Major bleeding	0.54 (0.43 – 0.67)
Minor bleeding	0.80 (0.65 – 0.99)

Laudani C, Capodanno D, et al. JACC Cardiovasc Interv. 2022;15:268-277

Discontinuation of aspirin

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

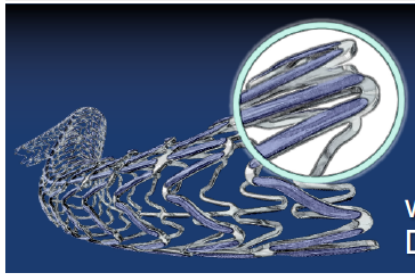
Post-interventional and maintenance treatment	Class	Level
After stent implantation in patients undergoing a strategy of DAPT, stopping aspirin after 3-6 months should be considered, depending on the balance between the ischaemic and bleeding risk.	IIa	A

Collet JP, Thiele H, et al. Eur Heart J. 2021;42:1289-1367

MASTER DAPT

Management of HBR Patients With an Abbreviated Versus Standard DAPT Regimen

INVESTIGATOR-INITIATED, OPEN LABEL, MULTICENTER, RANDOMIZED CONTROLLED TRIAL



4,579
HBR patients undergoing PCI with a BP-SES on DAPT for 1 month

	Abbreviated DAPT (SAPT for 11 mo [no OAC] or 5 mo [OAC]) N=2,295		Standard DAPT (DAPT for ≥5 mo [no OAC] or ≥2 mo [OAC]) N=2,284
Net adverse clinical events at 11 months (PP)	7.5%	Difference -0.23%, 2-sided 95% UCL 1.33%, P_{NI}<0.001	7.7%
All-cause death, MI, stroke (PP)	6.1%	P_{NI}=0.0014	5.9%
BARC type 2, 3, 5 bleeding (ITT)	6.5%	P<0.001	9.4%

One month of DAPT was noninferior to the continuation of therapy for at least 2 additional months

Valgimigli M, et al. N Engl J Med. 2021;385:1643-1655

Should we extend it?

Criteria for extended DAPT

ESC European Society of Cardiology

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

High thrombotic risk	High thrombotic risk	Moderate thrombotic risk

Complex CAD and at least 1 criterion:
• **Risk enhancers**
  • DM requiring medication
  • Recurrent MI
  • Multivessel CAD
  • CAD plus PAD
  • Premature or accelerated CAD
  • Inflammatory disease
  • CKD (eGFR 15-59 mL/min/1.73 m^2)
	Complex CAD and at least 1 criterion:
	• **Technical aspects**
	  • ≥3 stents implanted
	  • ≥3 lesions treated
	  • Total stent length >60 mm
	  • Complex PCI (left main, 2-stent bifurcation, CTO, last patent vessel)
	  • ST while on DAPT
		Non-complex CAD and at least 1 criterion:
		• **Risk enhancers**
		  • DM requiring medication
		  • Recurrent Mi
		  • CAD plus PAD
		  • CKD (eGFR 15-59 mL/min/1.73 m^2)

CTO, chronic total occlusion; GFR, glomerular filtration rate; LM, left main; PAD, peripheral artery disease.

Collet JP, *et al. Eur Heart J.* 2020;42(14):1289–1367.

Long-term DAPT

PEGASUS

MULTICENTER, RANDOMIZED, DOUBLE-BLIND

21,162 Patients with a MI within 1 to 3 years	Ticagrelor 60 mg bid	Matching placebo
MACE at 40 mo	7.8%	9.1%
	HR 0.84; P=0.004	
Major bleeding	2.3%	1.1%

Ticagrelor was more effective

N Engl J Med 2015; 372:1791-1800

THEMIS

MULTICENTER, RANDOMIZED, DOUBLE-BLIND

19,220 Patients ≥50 years who had stable CAD and type 2 diabetes mellitus	Ticagrelor 60 mg bid	Matching placebo
MACE at 36 mo	7.7%	8.5%
	HR 0.90; P=0.04	
Major bleeding	2.2%	1.0%

Ticagrelor was more effective

N Engl J Med 2019;381:1309-1320

COMPASS

MULTICENTER, RANDOMIZED, DOUBLE-BLIND

27,395 Patients with stable atherosclerotic vascular disease (CAD/PAD)	Rivaroxaban 2.5 mg bid	Matching placebo
MACE at 23 mo	4.1%	5.4%
	HR 0.76; P<0.001	
Major bleeding	3.1%	1.9%

Rivaroxaban was more effective

N Engl J Med 2017;377:1319-1330

Long-term DAPT or DPI

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Shortening antithrombotic treatment duration	Class	Level
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.	IIa	A
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.	IIb	A

Collet JP, Thiele H, et al. Eur Heart J. 2021;42:1289-1367

Should we modify it?

Unguided switch

TOPIC

SINGLE CENTER, RANDOMIZED, OPEN-LABEL

642 ACS-PCI patients after 1 mo of DAPT with prasugrel or ticagrelor	Switched (aspirin + clopidogrel)	Unchanged (same DAPT)
NACE at 12 mo	13.4%	26.3%
	HR 0.48 (0.34-0.68); P<0.01	
BARC ≥2 type bleeding	4.0% P<0.01	14.9%

Switched DAPT was superior to unchanged DAPT

Cuisset T, et al. Eur Heart J. 2017;38:3070-3078

TALOS-AMI

MULTICENTER, RANDOMIZED, OPEN-LABEL

2,697 AMI-PCI patients who received aspirin and ticagrelor for 1 mo	Switched (aspirin + clopidogrel)	Unchanged (same DAPT)
NACE at 1-12 mo	4.6%	8.2%
	HR 0.55 (0.40-0.76); P_{NI}<0.001	
BARC ≥2 type bleeding	3.0% P=0.0012	5.6%

Unguided de-escalation strategy was superior

Kim CJ, et al. Lancet. 2021;398:1305-1316

Guided switch

TROPICAL-ACS

MULTICENTER, RANDOMIZED, OPEN-LABEL

2,610 Patients with acute coronary syndromes undergoing PCI	PFT-guided clopidogrel (non-HPR)	Standard (prasugrel)
NACE at 12 mo	7%	9%
	HR 0.81 (0.62-1.06); P_{NI}=0.0004	
MACE	3% P_{NI}=0.01	3%

PFT-guided de-escalation noninferior

Sibbing D, et al. Lancet. 2017;390:1747-1757

POPULAR-GENETICS

MULTICENTER, RANDOMIZED, OPEN-LABEL

2,488 Patients undergoing primary PCI with stent implantation	Geno-guided clopidogrel (non-LOF)	Standard (newer $P2Y_{12}$-i)
NACE at 12 mo	5.1%	5.9%
	ARD 0.7 (-2.0 to 0.7); P_{NI}<0.001	
Bleeding	9.8% P=0.04	12.5%

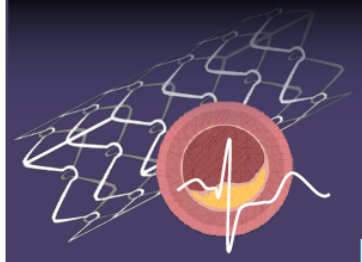
Genotype-guided de-escalation noninferior

Claassens DM, et al. N Engl J Med 2019;381:1621-1631

Halving the dose

Prasugrel-based de-escalation of DAPT after PCI in patients with ACS

HOST-REDUCE-POLYTECH-ACS | OPEN-LABEL, MULTICENTER, NONINFERIORITY RANDOMIZED TRIAL



2,338
Patients with acute coronary syndromes undergoing PCI on prasugrel 10 mg daily

	Dose adjustment (prasugrel 5 mg after 1 month) N=1,170		Standard DAPT (aspirin + prasugrel 10 mg) N=1,168
Death, MI, stroke, ST, revascularisation, BARC ≥2 bleeding at 1 year	7.2%		10.1%
	ARD -2.9%, P_{NI}<0.0001; HR 0.70 [95% CI 0.52-0.92], P_{EQ}=0.012		
MACE	1.4%	P=0.40	1.8%
BARC ≥2 bleeding	2.9%	P<0.0007	4.9%

A prasugrel-based dose de-escalation strategy from 1 month after PCI reduced the risk of NACE up to 1 year

Kim HS, et al. Lancet 2020;396:1079-1089

De-escalation

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

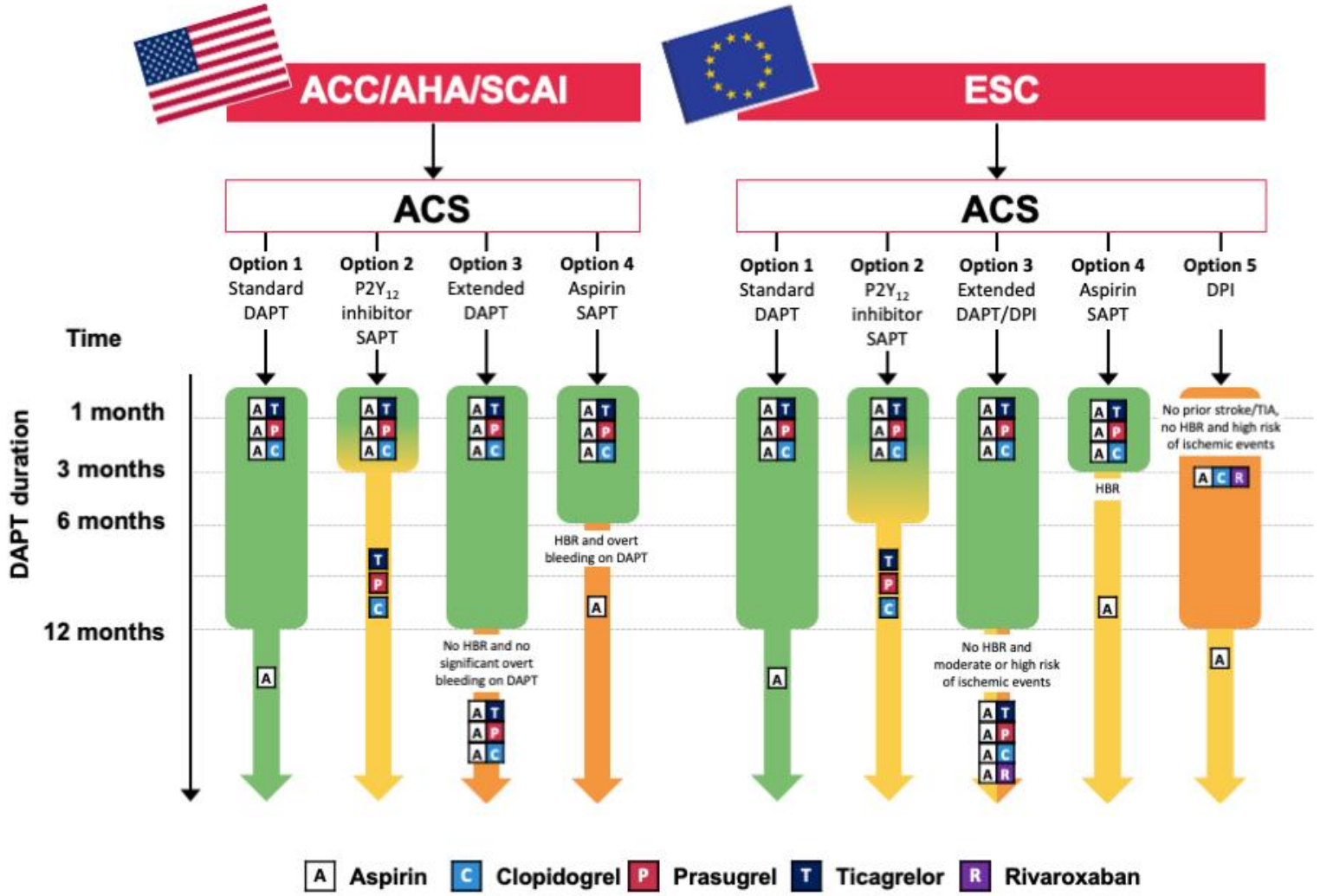
Shortening antithrombotic treatment duration	Class	Level
De-escalation of $P2Y_{12}$ receptor inhibitor treatment (e.g., with a switch from prasugrel or ticagrelor to clopidogrel) may be considered as an alternative DAPT strategy, especially for ACS patients deemed unsuitable for potent platelet inhibition. De-escalation may be done unguided based on clinical judgment or guided by platelet function testing or CYP2C19 genotyping, depending on patient's risk profile and availability of respective assays.	IIb	A

Collet JP, Thiele H, et al. Eur Heart J. 2021;42:1289-1367

Conclusions DAPT et ACS

- Très haut risque hémorragique
  - 1 mois →(MASTER-DAPT)?
- Haut risque hémorragique
  - 3 à 6 mois
  - Arrêt → de préférence l'aspirine et relais vers le clopidogrel
- Risque standard
  - 12 mois
  - Réduire l'intensité au bout de 1 à 3 mois
- Risque ischémique ↗ ou ↗↗ et faible risque hémorragique
  - Poursuivre au-delà de 12 mois
  - Ajouter faible dose de rivaroxaban à l'aspirine

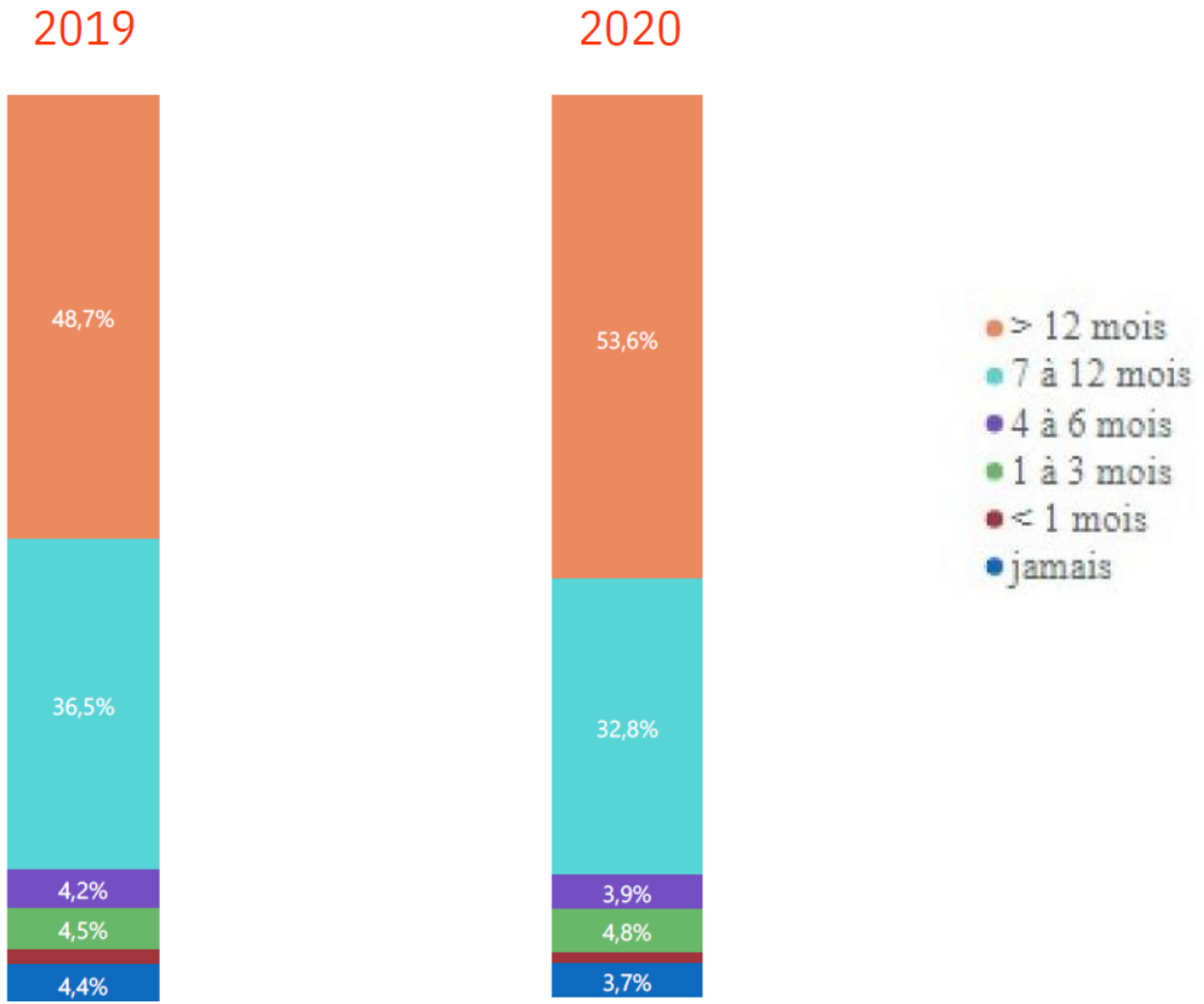
Reco ACS actuelles



Eur. Heart J. **42**, 1289–1367 (2021); *J Am Coll Cardiol. 2022 Jan 18;79(2):197-215*

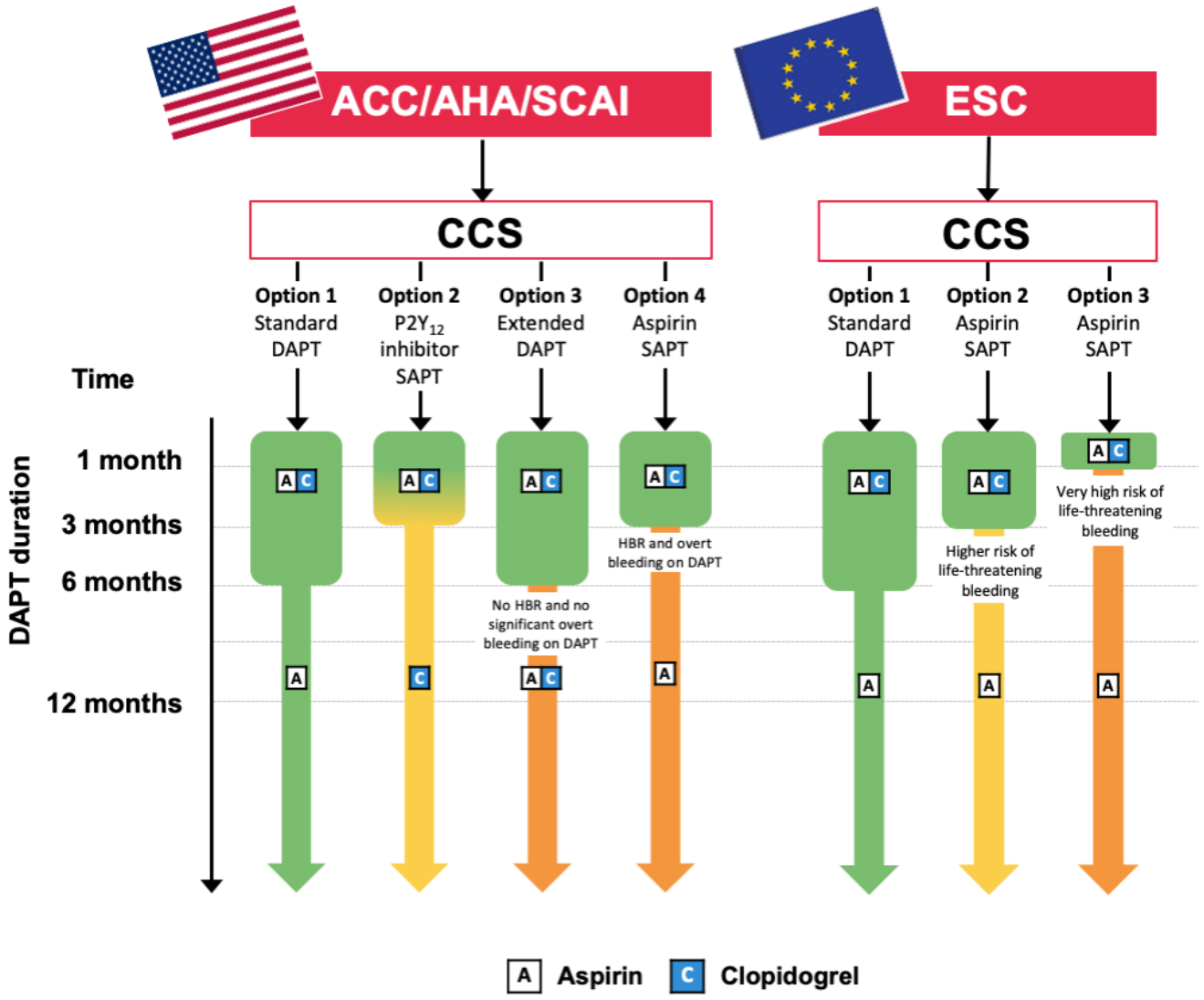
France PCI_STEMI

Moyenne France PCI



Chronic coronary syndrome

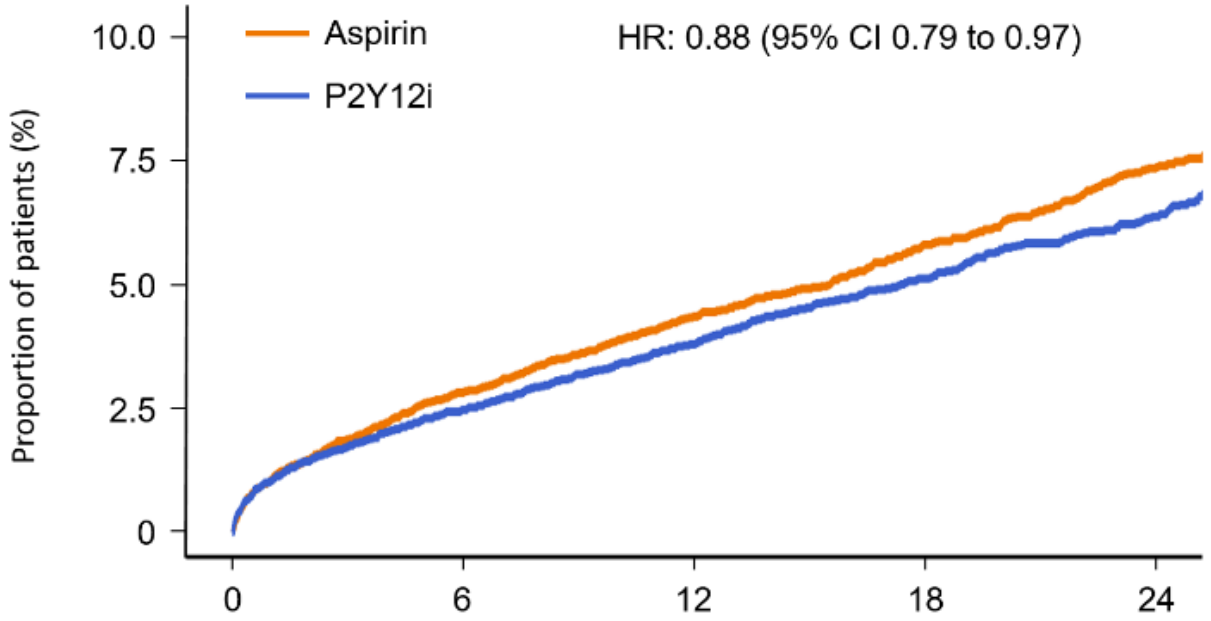
Reco CCS actuelles



Eur. Heart J. **42**, 1289–1367 (2021); *J Am Coll Cardiol. 2022 Jan 18;79(2):197-215*

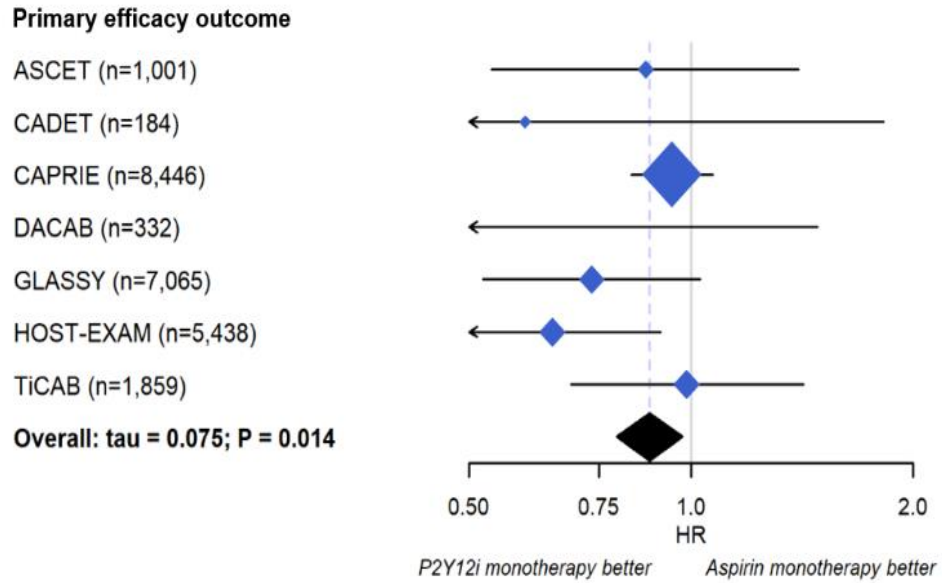
Aspirin or clopidogrel?

CV death, MI or stroke: 5.5% vs. 6.3%; HR 0.88, 95% CI 0.79 to 0.97, P=0.014; NNTB: 123



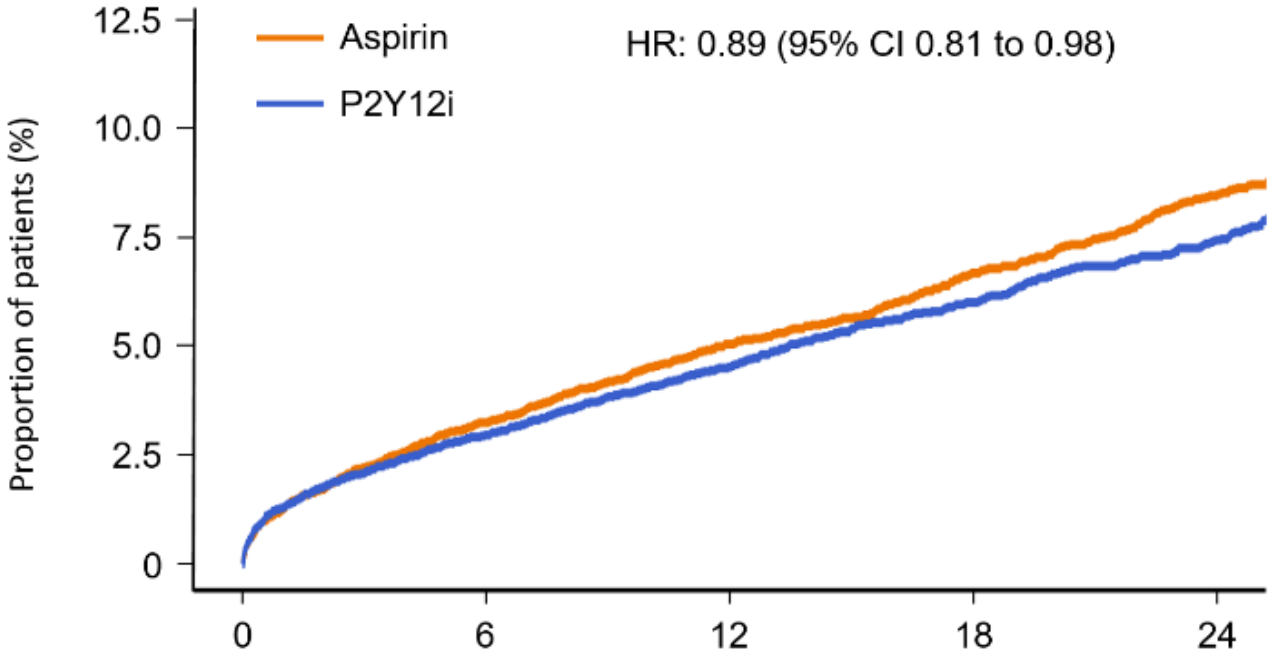
Number at risk

Aspirin	11645	11143	10141	5405	4288
P2Y12i	11679	11196	10142	5389	4357



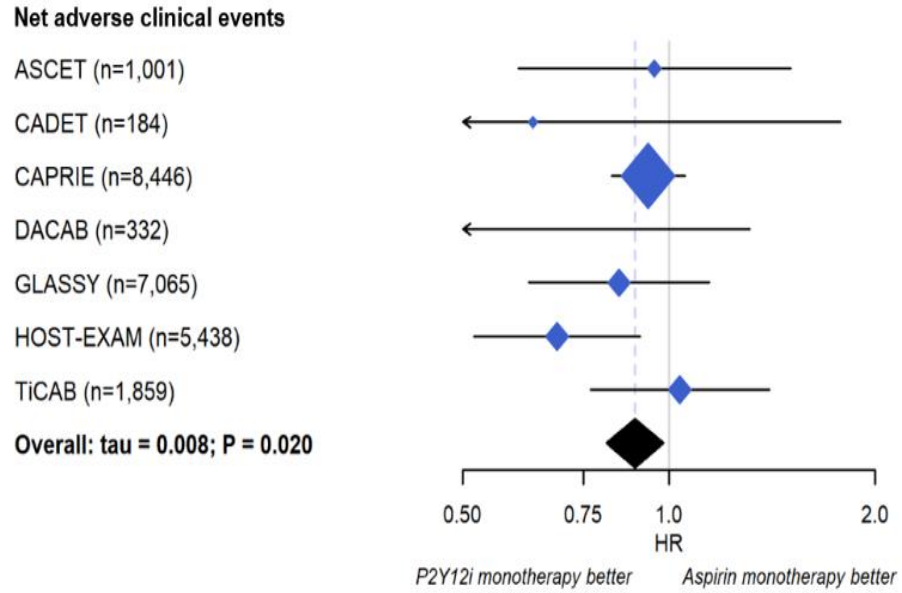
Aspirin or clopidogrel?

NACE: 6.4% vs. 7.2%; HR 0.89, 95% CI 0.81 to 0.98, P=0.02



Number at risk

Aspirin	11479	10935	9949	5363	4244
P2Y12i	11513	10987	9959	5354	4323

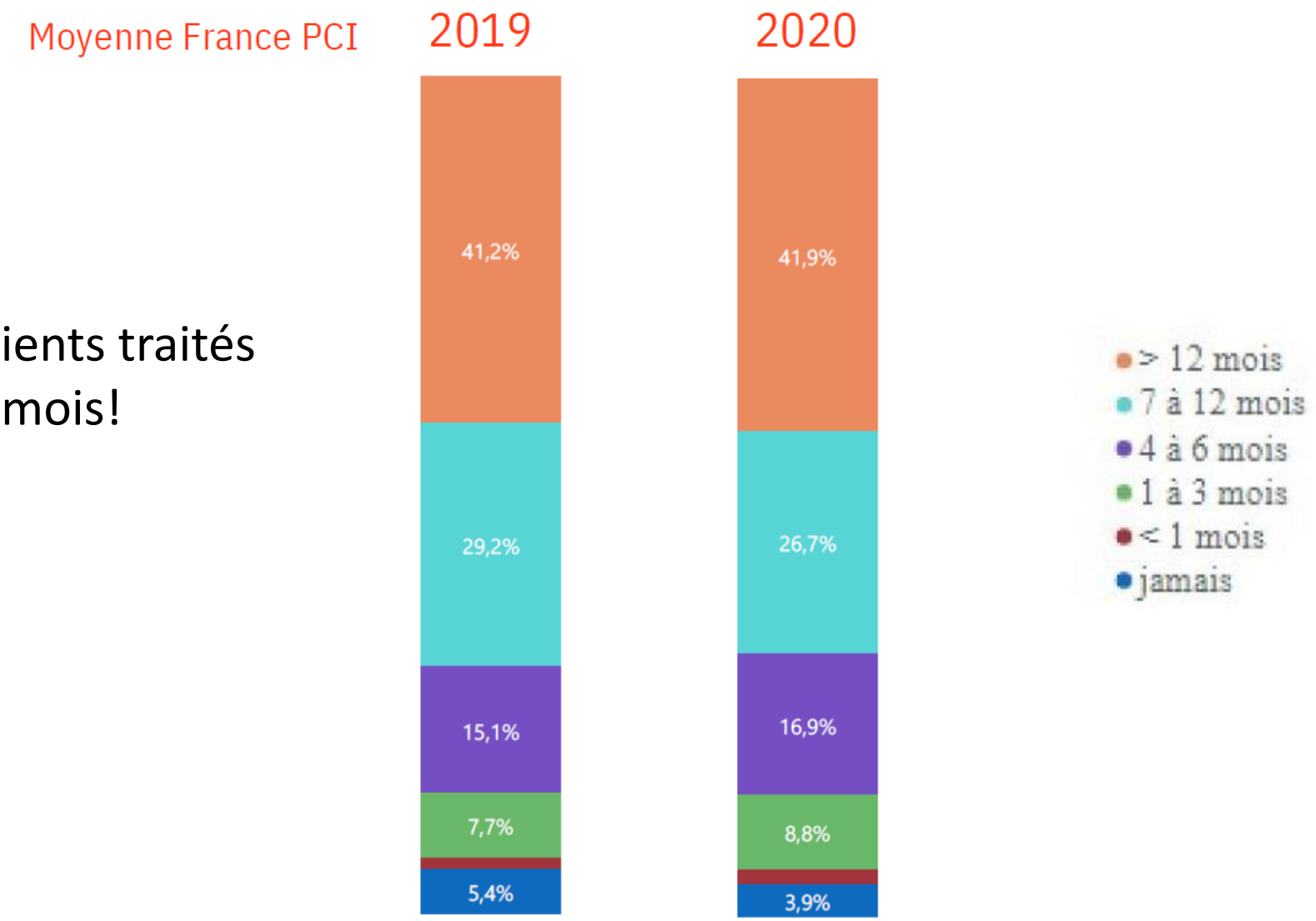


Conclusions DAPT et CCS

- Très haut risque hémorragique
  - 1 mois
- Haut risque hémorragique
  - 3 mois
  - Arrêt → de préférence l'aspirine et relais vers le clopidogrel
- Risque standard
  - 6 mois
  - Arrêt → de préférence l'aspirine et relais vers le clopidogrel

France PCI

¾ des patients traités plus de 6 mois!



Thank you