TCTAP 2021
VIRTUAL

APRIL 21-24, 2021

Short DAPT Followed by $P2Y_{12}$ Monotherapy: New Trend Updates with Clinical Evidences

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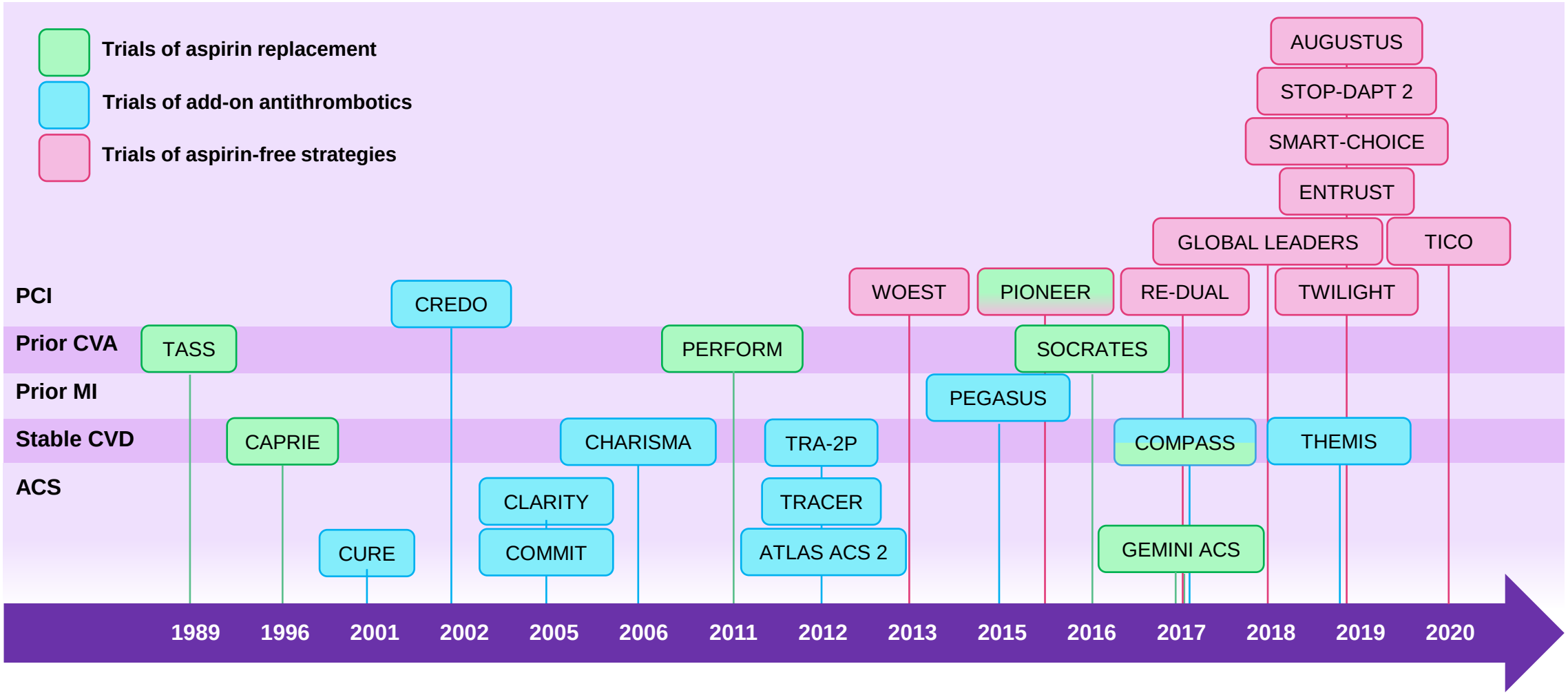
February 16, 2021

Evolving paradigms



Capodanno D, Angiolillo DJ, et al. Nat Rev Cardiol. 2018;15:480-496

Dropping aspirin, why?

1. Bleeding risk

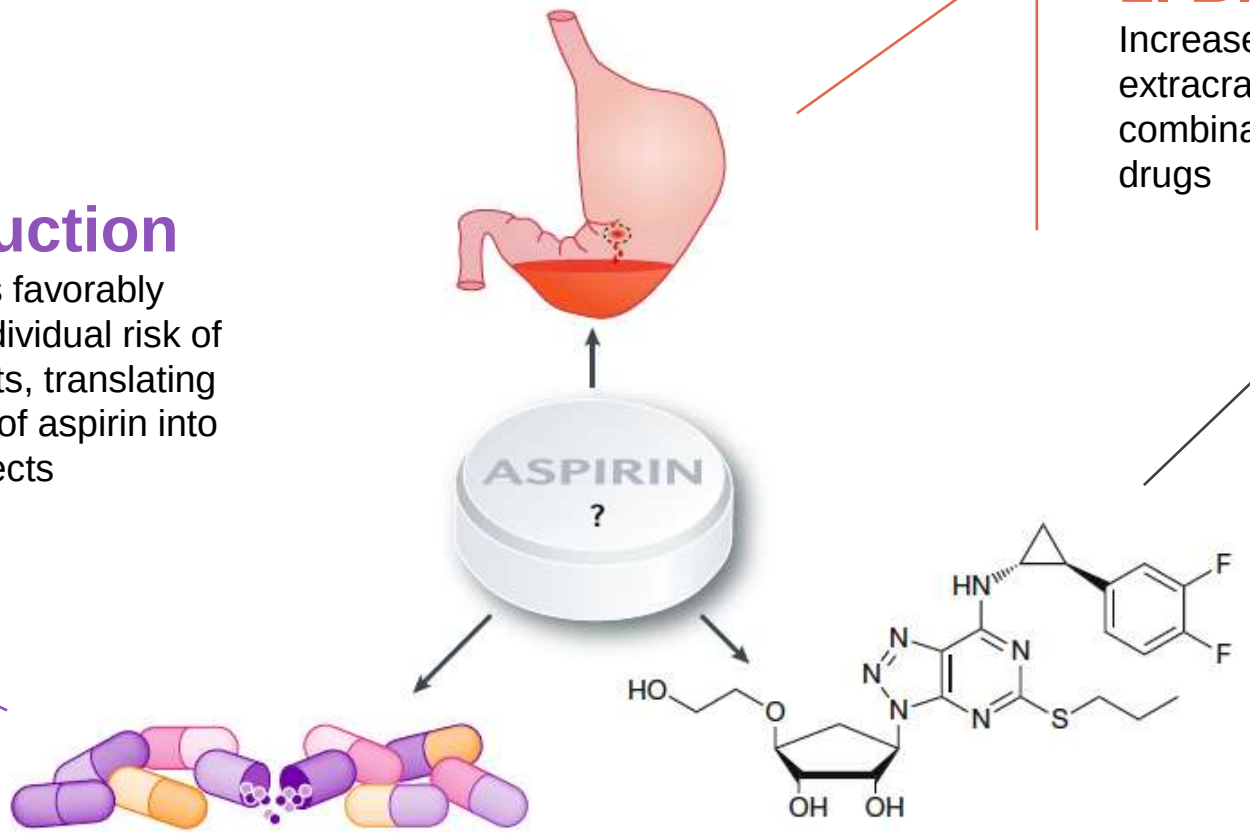
Increased risk of intracranial and extracranial bleeding, especially in combination with other antithrombotic drugs

2. Novel drugs

The availability of new compounds with potent antithrombotic efficacy could make the use of aspirin no longer necessary

3. Risk reduction

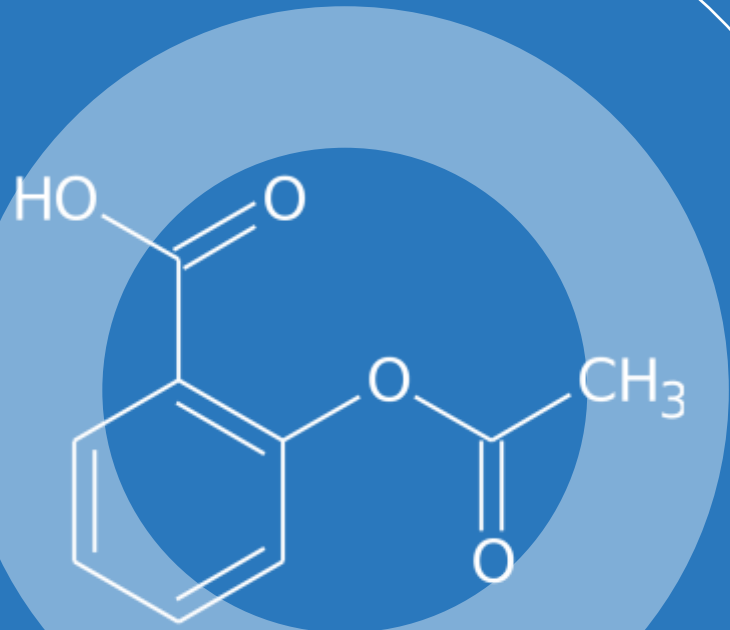
Contemporary drugs favorably alter the baseline individual risk of cardiovascular events, translating the relative benefits of aspirin into smaller absolute effects



Capodanno D, Angiolillo DJ, et al. Nat Rev Cardiol. 2018;15:480-496

1 CLINICAL EVIDENCE IN PCI AND ACS POPULATIONS

RANDOMIZED TRIALS OF ASPIRIN-FREE STRATEGIES



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GLOBAL LEADERS

GLOBAL LEADERS		
N=15,968 (PCI)	**Ticagrelor alone at 3 mo**	**DAPT for 12 mo (► ASA)**
All-cause death or new Q-wave MI at 2 years	**3.81%**	**4.37%**
	Rate ratio 0.87; 95% CI 0.75-1.01; P=0.073	

GLOBAL LEADERS Adjudication Sub-Study (GLASSY)		
N=7,585 (PCI)	**Ticagrelor alone at 3 mo**	**DAPT for 12 mo (► ASA)**
All-cause death, MI, stroke or TVR at 2 years	**7.14%**	**8.41%**
	Rate ratio 0.85; 95% CI 0.72-0.99; P_{NI}=0.001; P_{SUP}=NS	

Vranckx P, et al. Lancet. 2018;392:940-949; Franzone A, et al. J Am Coll Cardiol. 2019;74:2223-2234

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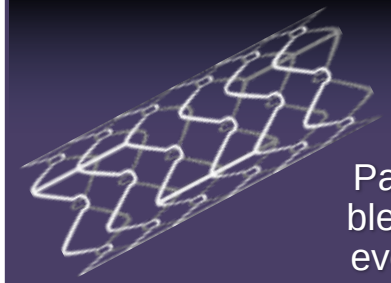
TWILIGHT

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

DOUBLE-BLIND, MULTICENTER, SUPERIORITY RANDOMIZED TRIAL



7,119
Patients at high risk for bleeding or an ischemic event at 3-mo from PCI

	Ticagrelor + Placebo (90 mg bid twice daily) N=3,555	Ticagrelor + Aspirin (90 mg twice daily + 81-100 mg daily) N=3,564
BARC 2, 3, or 5 bleeding at 12 months	4.0%	7.1%
	Hazard ratio 0.56; 95% CI 0.45-0.68; P<0.001	
All-cause death, MI or stroke	3.9%	3.9%
	P_{NI}<0.001	

Ticagrelor monotherapy was associated with a lower incidence of clinically relevant bleeding

Mehran R, et al. N Engl J Med. 2019;381:2032-2042

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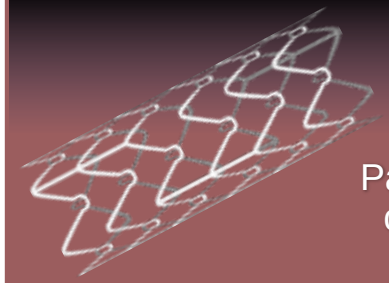
TICO

Ticagrelor with or without Aspirin in Patients with Acute Coronary Syndromes

OPEN-LABEL, MULTICENTER, SUPERIORITY RANDOMIZED TRIAL



3,056
Patients with an acute coronary syndrome undergoing PCI

	Experimental strategy (3-mo DAPT followed by ticagrelor alone) N=1,527	Control strategy (Ticagrelor + aspirin) N=1,529	
Net adverse cardiac events at 12 months	3.9%	5.9%	Hazard ratio 0.66; 95% CI 0.48-0.92; P=0.01
Major bleeding	1.7%	3.0%	P=0.02

Ticagrelor monotherapy resulted in a modest but statistically significant reduction in NACE at 1 year

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

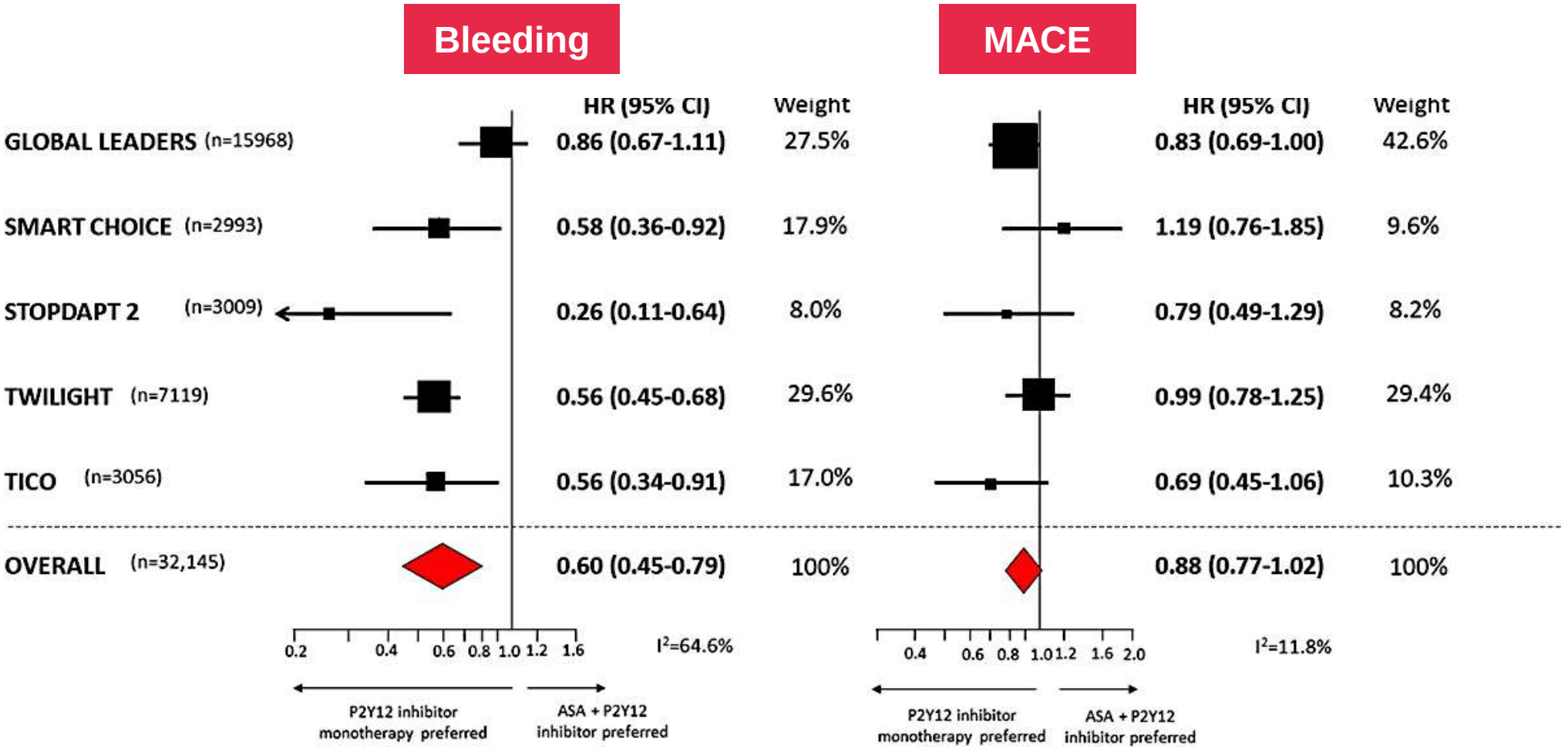
Clopidogrel monotherapy

STOPDAPT-2		
N=3,045 (PCI)	**Clopidogrel alone at 1 mo**	**DAPT**
NACE at 12 months	**2.4%**	**3.7%**
	Hazard ratio 0.64; 95% CI 0.42-0.98; P_{NI}<0.001; P_{SUP}=0.04	

SMART-CHOICE		
N=2,993 (PCI)	**Clopidogrel alone at 3 mo**	**DAPT**
MACE at 12 months	**2.9%**	**2.5%**
	Difference 0.4%; 1-sided 95% CI, -∞% to 1.3%; P_{NI}=0.007	

Watanabe H, et al. JAMA. 2019;321:2414-2427; Hahn JY, et al. JAMA. 2019;321:2428-2437

Putting all together

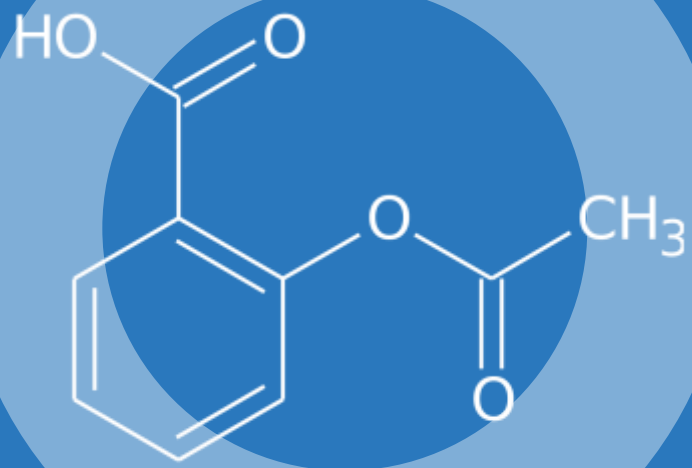


O' Donoghue ML, et al. Circulation. 2020;142:538–545

2

PHARMACODYNAMIC CONSIDERATIONS

DROPPING ASPIRIN VS DROPPING $P2Y_{12}$ INHIBITORS



Building PD evidence

CONCLUSIONS

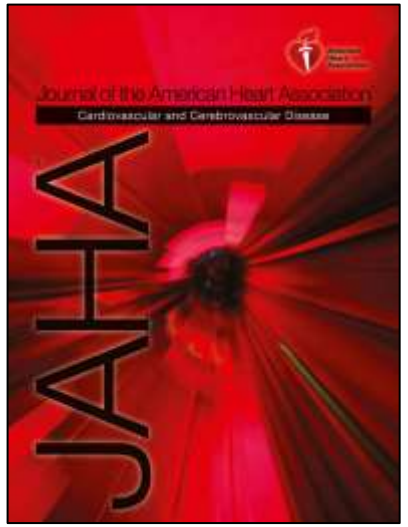
Strong $P2Y_{12}$ receptor blockade alone causes inhibition of platelet aggregation that is little enhanced by aspirin

CONCLUSIONS

The antithrombotic potency of ticagrelor monotherapy is similar to that of ticagrelor and aspirin with respect to blood thrombogenicity

CONCLUSIONS

Cessation of either component of DAPT leads to substantial increase in platelet reactivity with differential effects on different pathways



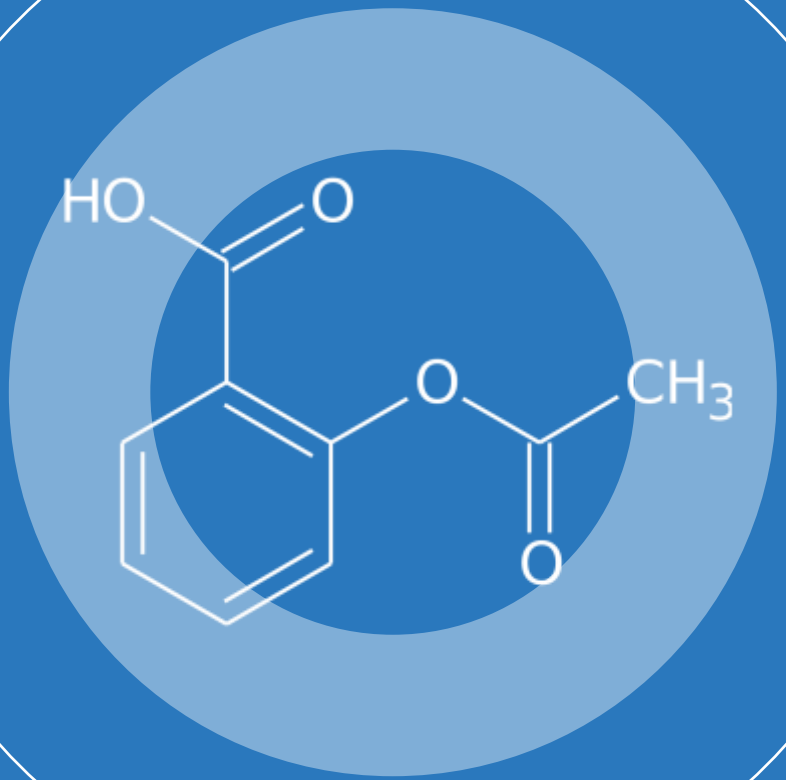
CONCLUSIONS

Incomplete inhibition of GPVI receptor-mediated platelet activation may contribute to the lower bleeding rates observed with ticagrelor compared with DAPT

Armstrong PC, et al. J Thromb Haemost. 2011;9:552-61; Baber U, et al. J Am Coll Cardiol. 2020;75:578-586; Hennigan BW, et al. Platelets. 2020: online ahead of print; Johnson TW, et al. J Am Heart Assoc. 2020;9:e016495

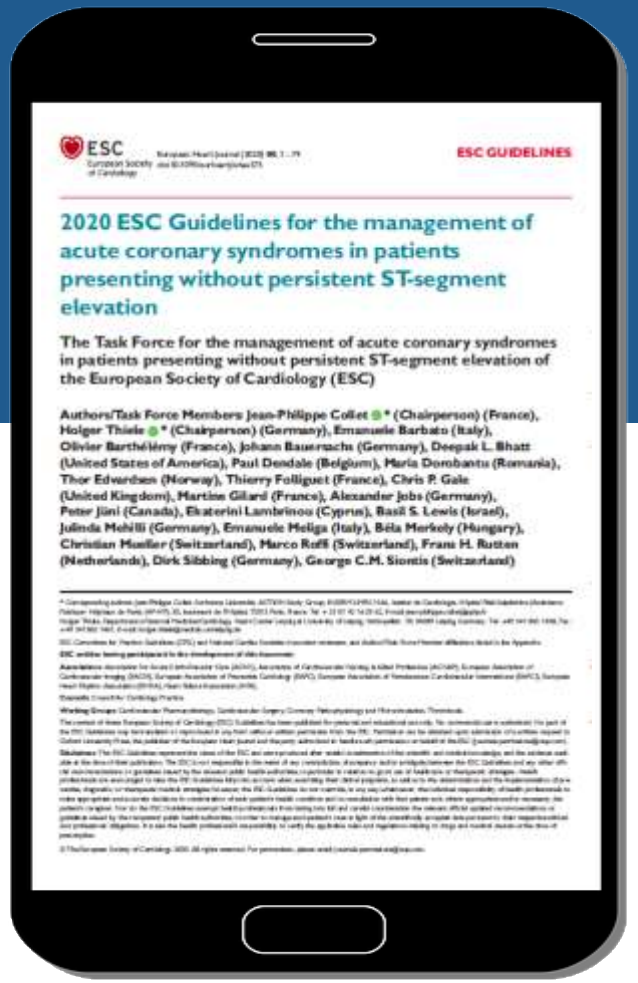
3 GUIDELINES AND FUTURE DIRECTIONS

RECOMMENDATIONS AND ONGOING TRIALS



2020 ESC Guidelines for ACS Without ST Elevation

Antiplatelet Therapy



Recommendations

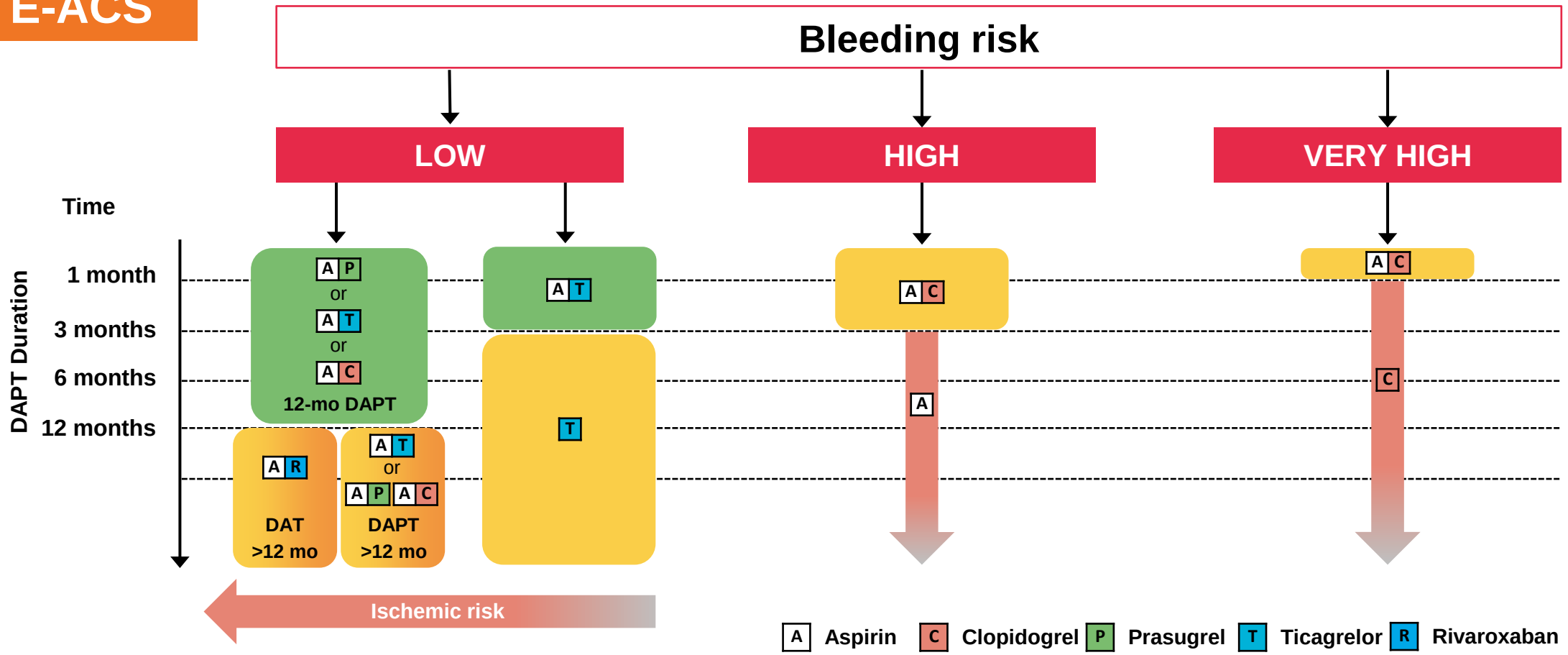
After stent implantation in patients undergoing a strategy of DAPT, stopping aspirin after 3-6 months should be considered, depending on the balance between the ischaemic and bleeding risk.

Class	Level
IIa	A

Collet JP, et al. Eur Heart J 2020 [ahead of print]

Duration of DAPT

NSTE-ACS



Collet JP, et al. Eur Heart J 2020 [ahead of print]

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Ongoing trials

Study name	n	Study population	Study intervention	Primary outcome(s)
OPT-BIRISK	7,700	ACS and PCI (9-12 mo of DAPT)	Clopidogrel SAPT	BARC 2-5 at 9 mo
SMART-CHOICE 3	5,000	Prior PCI (≥12 months)	Clopidogrel SAPT	MACCE at 12 mo
STOPDAPT-2 ACS	3,008	ACS and PCI	Clopidogrel SAPT	NACE at 12 and 60 mo
NEOMINDSET	3,400	ACS and PCI	Prasugrel or Ticagrelor SAPT	MACCE at 12 mo BARC 2-5 at 12 mo
A-CLOSE	3,200	PCI (12 mo of DAPT)	Clopidogrel SAPT	NACE between 12 and 36 mo
IVUS-ACS and ULTIMATE-DAPT	3,486	ACS and PCI	Ticagrelor SAPT	BARC 2-5 and MACCE between 1 and 12 mo
SMART-CHOICE 2	1,520	PCI (12 mo of DAPT)	Clopidogrel or low-dose ticagrelor SAPT	MACCE between 12 and 36 mo

Cao D, et al. Eur Heart J. 2020:ehaa824 [ahead of print]

CLOSING REMARKS

Short DAPT Followed by P2Y12 Monotherapy: New Trend Updates with Clinical Evidences

- Aspirin has been for years the background therapy of several investigations of new antithrombotic drugs or strategies. This paradigm is changing.
- There is little apparent pharmacodynamic benefit in adding aspirin to prasugrel or ticagrelor.
- Among selected patients with and without ACS undergoing PCI and who have completed a short term of DAPT with a $P2Y_{12}$ inhibitor plus aspirin, dropping aspirin may significantly lower the risk of clinically important bleeding without increasing the risk for ischemic events.

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