

# Recommendation Guided *versus* Potent P2Y12 Inhibitor Therapy: updated evidence

Dr. Pieter C. Smits

Head of Interventional Cardiology  
Department

Maasstad Ziekenhuis;

Rotterdam

The Netherlands



# Current EU/US guidelines recommendations post PCI<sup>1,2</sup>

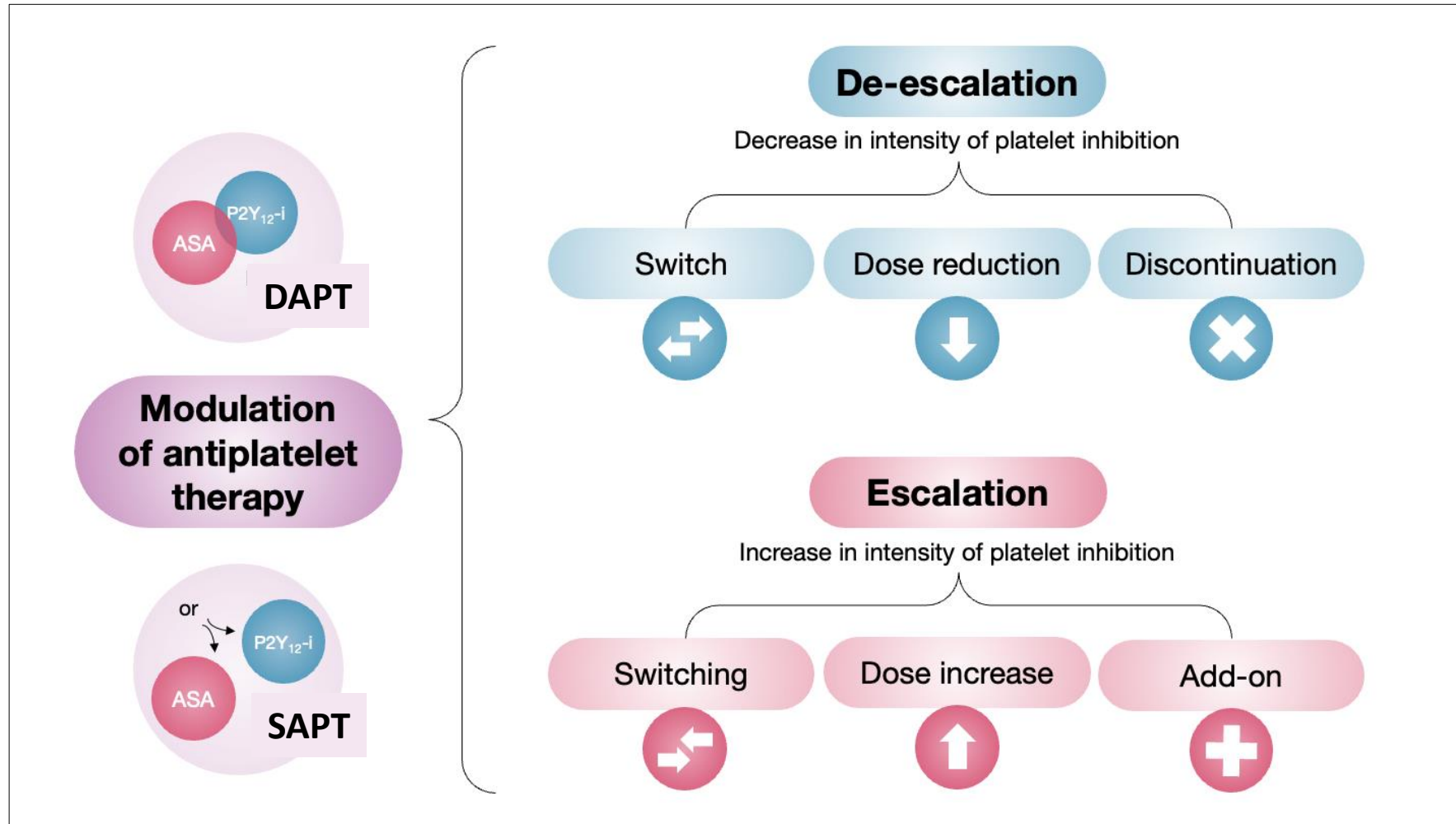
ACS => DAPT (ASA + Potent P2Y12i)  $\geq$  12 months

CCS => DAPT (ASA + Clopidogrel)  $\leq$  6 months

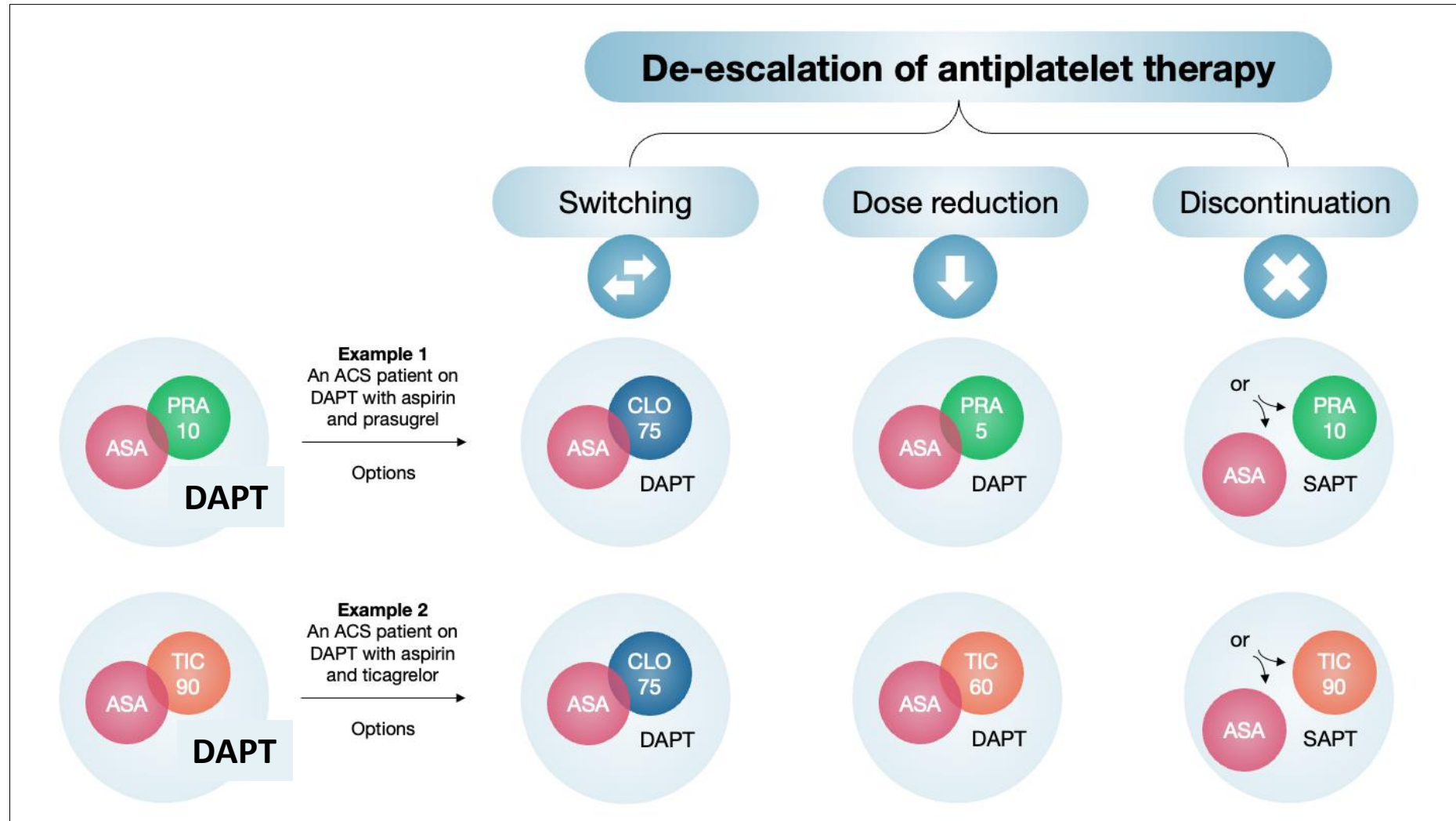
} DAPT period followed by SAPT (ASA)

Current recommendation are well defined and represent an effective treatment strategy for most patients, unless bleeding or ischemic or both risk prevails

# New ARC initiative: Consensus Document on Defining Strategies of Antiplatelet Modulation<sup>1</sup>

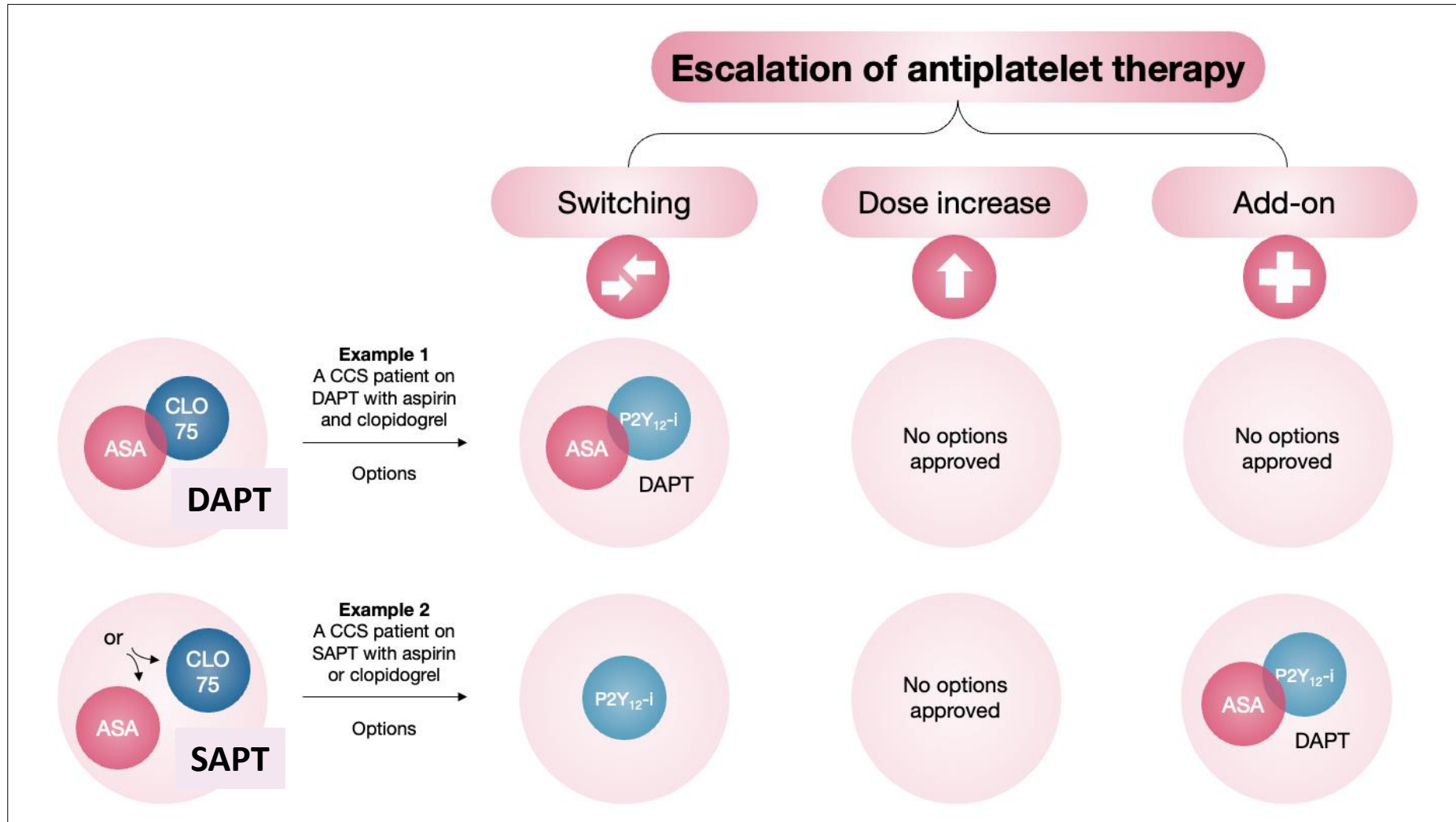


# New ARC initiative: Consensus Document on Defining Strategies of Antiplatelet Modulation<sup>1</sup>

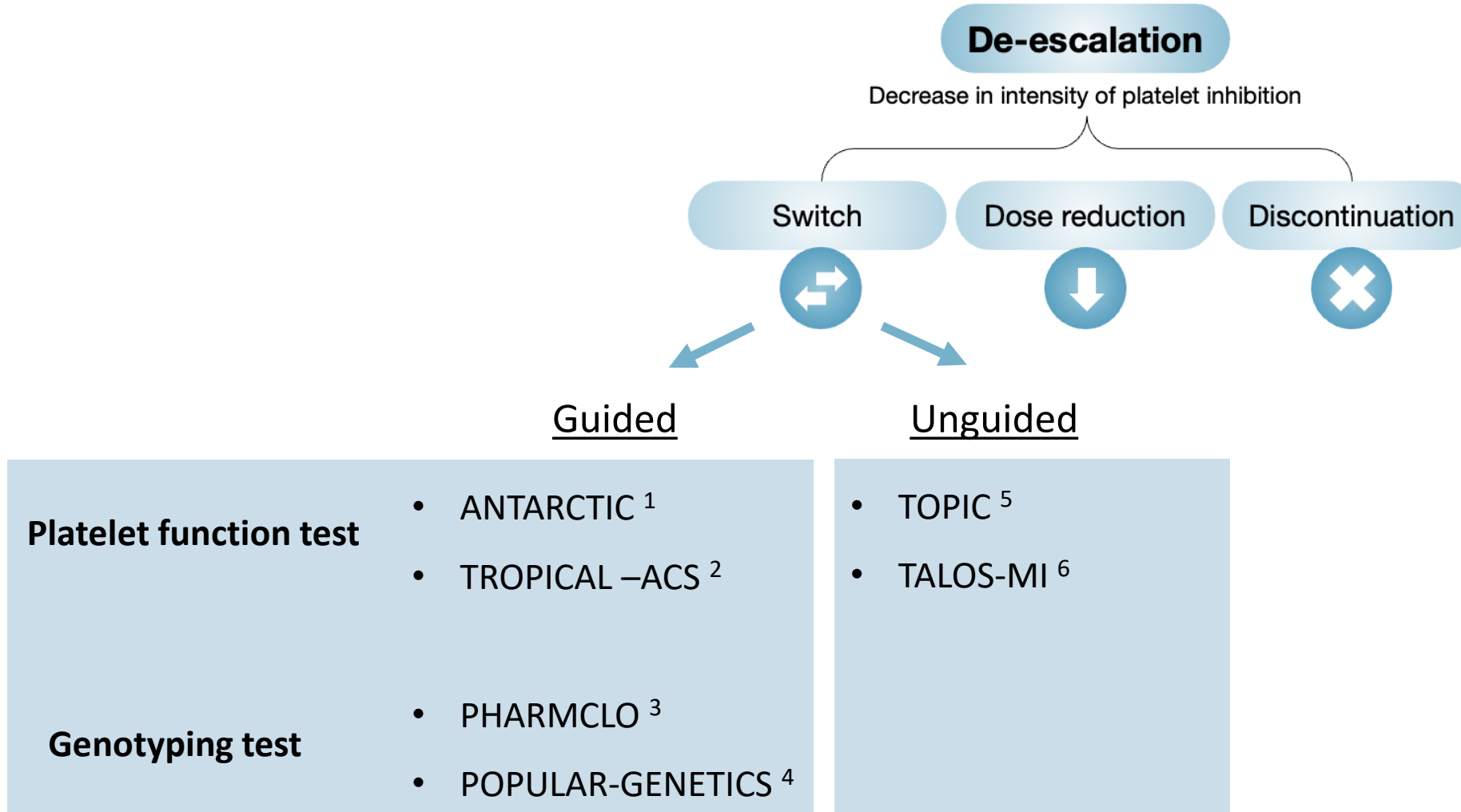




# New ARC initiative: Consensus Document on Defining Strategies of Antiplatelet Modulation<sup>1</sup>



# De-escalation by Guided and Unguided Switch



1. Cayla et al. ANTARCTIC Lancet 2016  
2. Siibbing et al. TROPICAL-ACS Lancet 2017

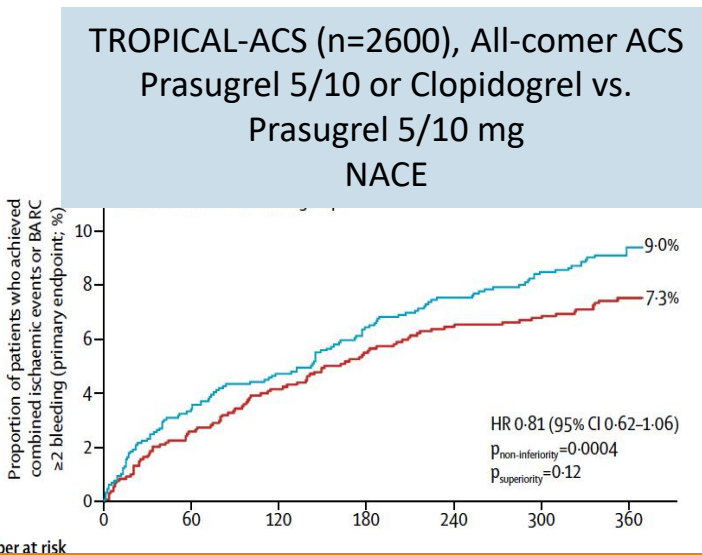
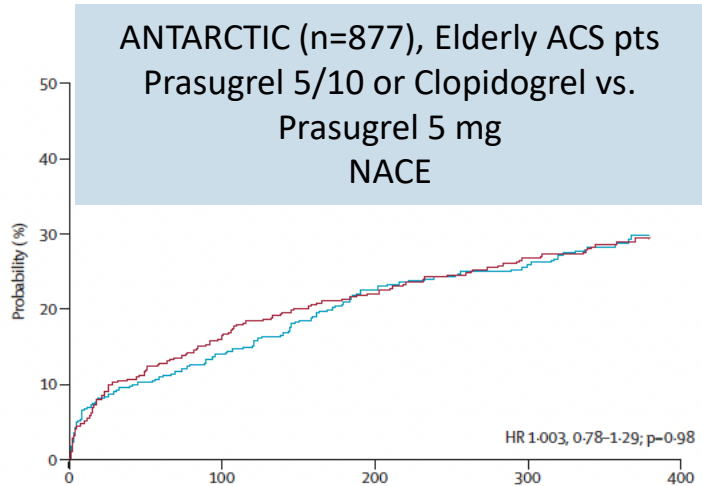
3. Notarangelo et al. PHARMCLO JACC 2018  
4. Claassens et al. POPULAR-GENETICS NEJM 2019

5. Cuisset et al. TOPIC EHJ 2018  
6. Kim et al. TALOS-MI Lancet 2021

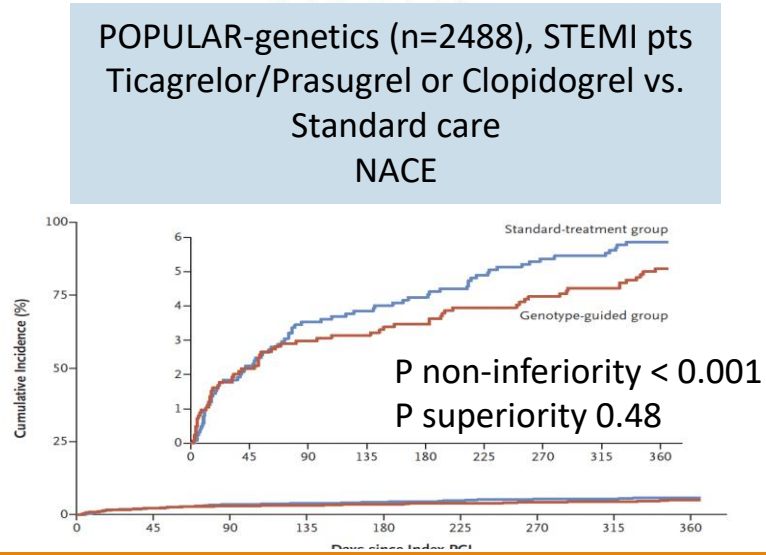
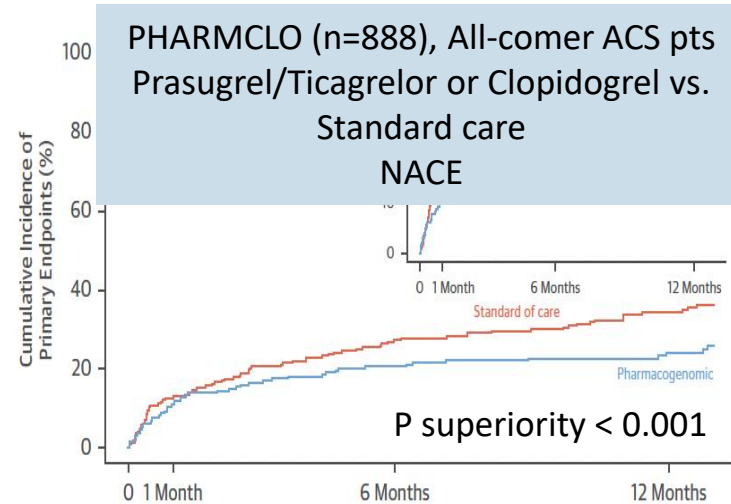
# De-escalation: Guided and Unguided Switch

## Guided

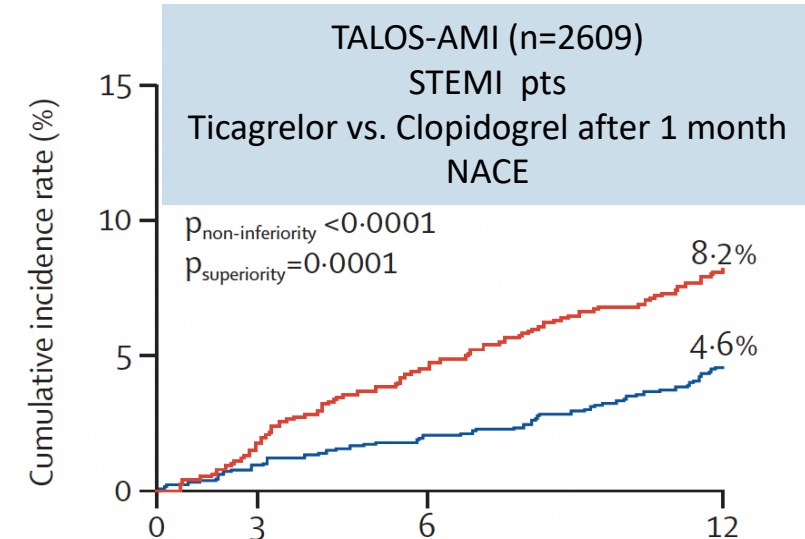
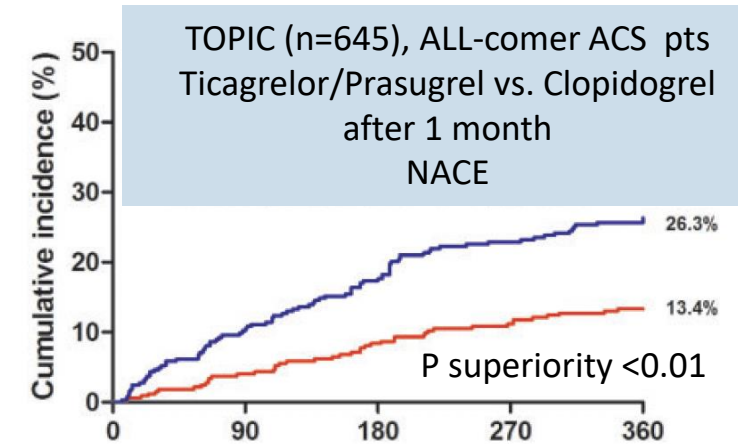
Platelet reactivity



Genotyping



## Unguided



1. Cayla et al. ANTARCTIC Lancet 2016
2. Siibing et al. TROPICAL-ACS Lancet 2017

3. Notarangelo et al. PHARMCLO JACC 2018
4. Claassens et al. POPULAR-GENETICS NEJM 2019

5. Cuisset et al. TOPIC EHJ 2018
6. Kim et al. TALOS-MI Lancet 2021

## Conclusions

### De-escalating by Guided and Unguided Switch

---

- ❖ De-escalating by switch consist of changing an antiplatelet drug by another one with the intention to decrease the antiplatelet inhibitory effect
- ❖ Current RCT's show mixed effect on NACE. Some no effect or non-inferiority, some superiority (PHARMCLO, TOPIC and TALOS-AMI), though all RCT's show safety and 5 out of 6 show significant reduction with bleeding
- ❖ More data is needed on comparison guided versus unguided, optimal timing of de-escalating by switch and which subgroups might benefit or not



# Current EU/US guidelines recommendations for Switching<sup>1,2</sup>



De-escalation of P2Y<sub>12</sub> 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.<sup>218,220,221</sup>

**IIb**

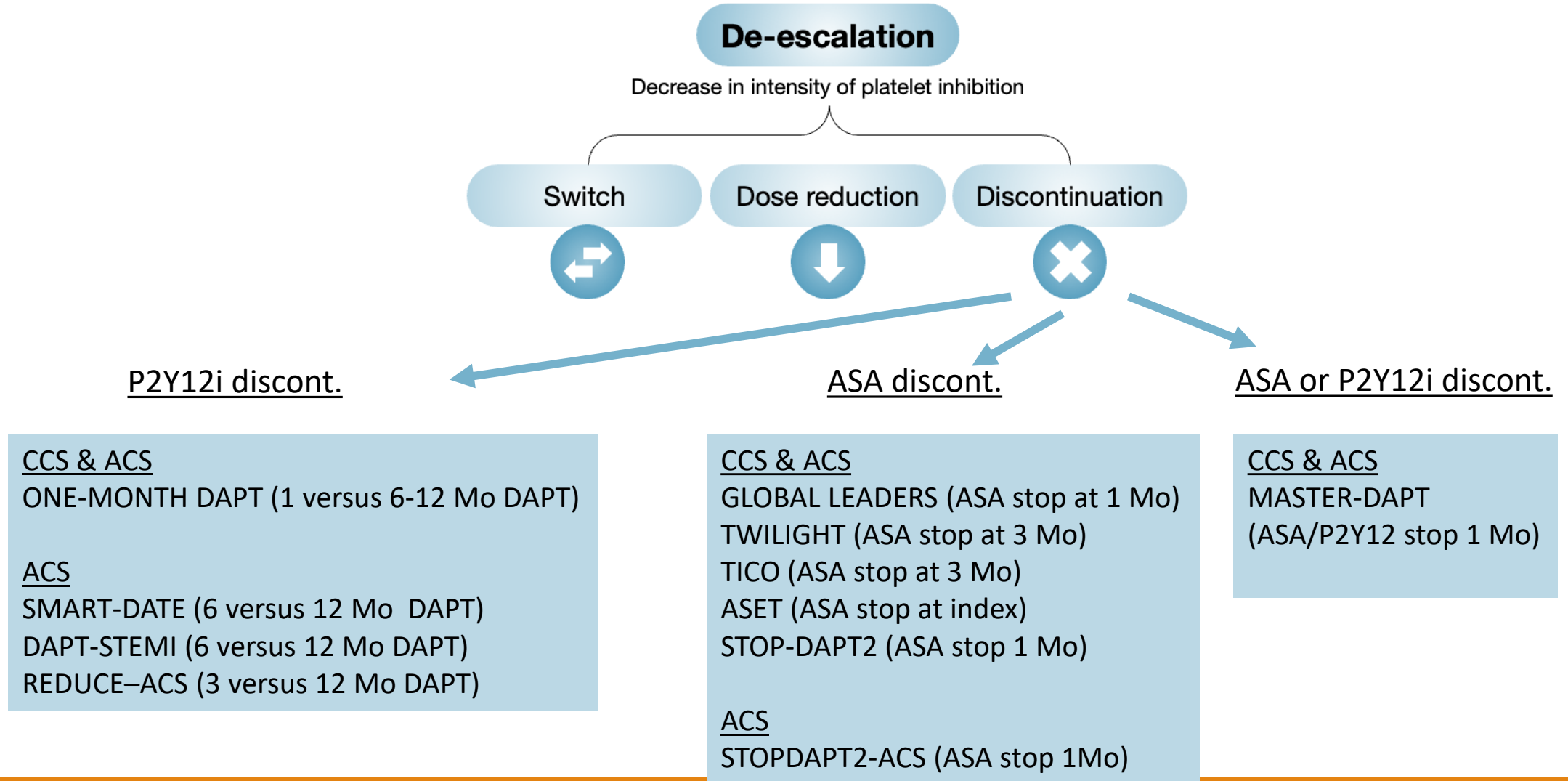
**A**



The 2021 joint guidelines from the American College of Cardiology (ACC), American Heart Association (AHA) and Society for Cardiovascular Angiography and Interventions (SCAI) do not mention de-escalation by switching among the options to reduce bleeding after PCI<sup>2</sup>.

1. Collet et al. 2020 ESC Guidelines for the management of NSTEMI. Eur Heart J 2021;42:1289–1367
2. Lawton et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization. Circulation 2021

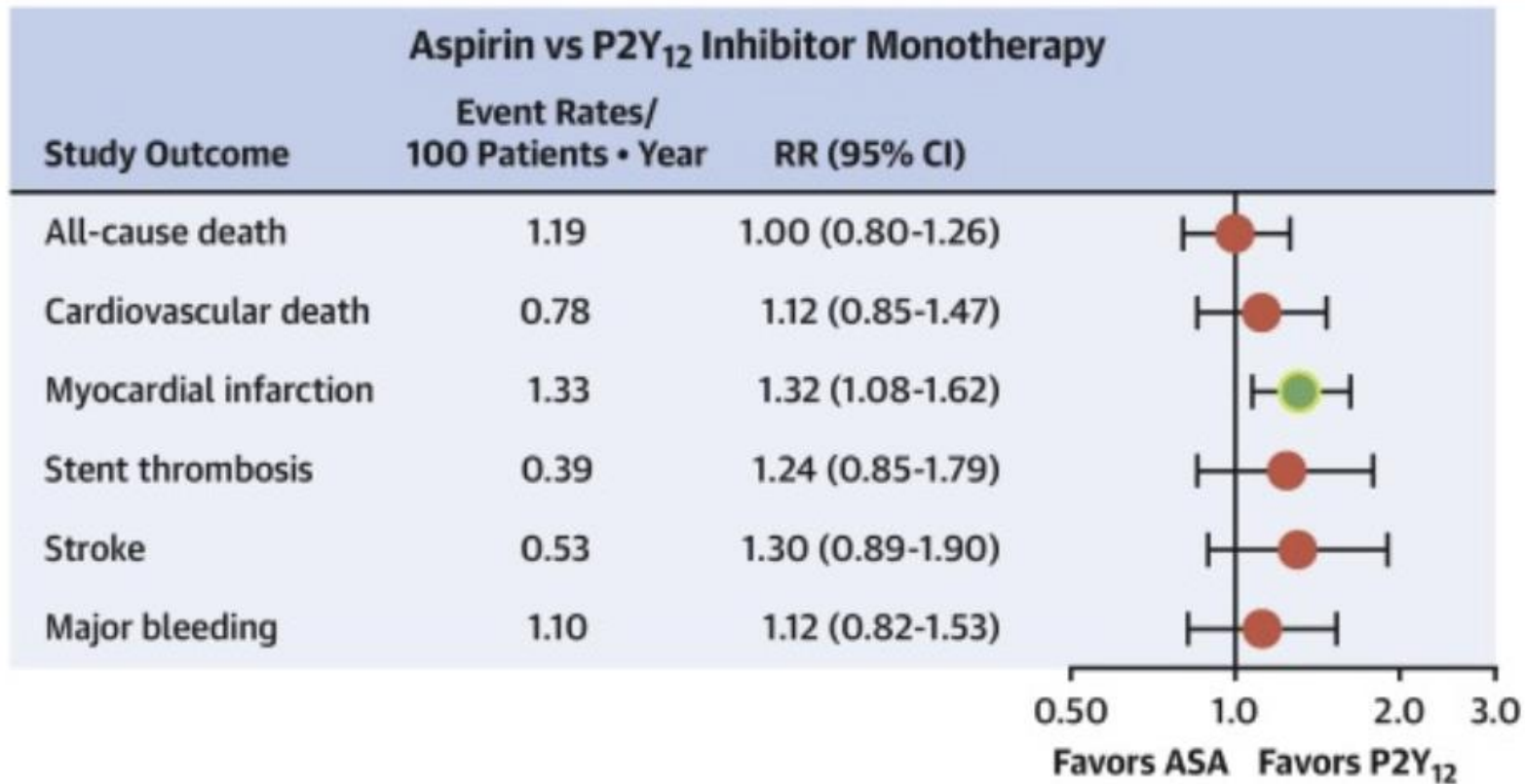
# De-escalation by Discontinuation



SMART-CHOICE	Xience	All	3 months DAPT	P2Y <sub>12</sub> inhibitor
EVOLVE Short DAPT	Synergy	HBR	3 months DAPT	
XIENCE 90	Xience	HBR	3 months DAPT	
TICO	Osiro	ACS	3 months DAPT	P2Y <sub>12</sub> inhibitor
TWILIGHT	All DES	High risk PCI	3 months DAPT	P2Y <sub>12</sub> inhibitor
MODEL U-SES	Ultimaster	All	3 months DAPT	
ISAR-DAPT	Coroflex	Low risk CAD	3 months DAPT	
HOST-IDEA	Osiro/Coroflex	Stable CAD	3 months DAPT	
SENIOR	Synergy	Age ≥ 75 yr	1 month DAPT	(SCAD arm)
GLOBAL LEADERS	Biomatrix	All-comers	1 month DAPT	P2Y <sub>12</sub> inhibitor
STOPDAPT-2	Xience	After PCI	1 month DAPT	P2Y <sub>12</sub> inhibitor
STOPDAPT-2 ACS	Xience	ACS	1 month DAPT	P2Y <sub>12</sub> inhibitor
POEM	Synergy	HBR	1 month DAPT	
XIENCE 28	Xience	HBR	1 month DAPT	
ONYX-ONE	Osiro	HBR	1 month DAPT	P2Y <sub>12</sub> inhibitor or ASA
MASTER-DAPT	Ultimaster	HBR (Including OAC)	1 month DAPT	P2Y <sub>12</sub> inhibitor or ASA
COMPARE 60/80 HBR	Ultimaster/Supraflex	HBR (including OAC)	1 month DAPT	P2Y <sub>12</sub> inhibitor or ASA
TARGET FIRST	Firehawk	ACS	1 month DAPT	P2Y <sub>12</sub> inhibitor
COMPARE STEMI ONE	Xience	STEMI	1 month DAPT	P2Y <sub>12</sub> inhibitor
COBRA-REDUCE	Cobra P2F	OAC	2 weeks DAPT	
ASET	Synergy	Low risk CAD	No DAPT	P2Y <sub>12</sub> inhibitor
ASET JAPAN	Synergy	CCS & NSTEMI-ACS	No DAPT	P2Y <sub>12</sub> inhibitor (Prasugrel)
NEO-MINDSET (3400 pts)	DES	ACS	No DAPT	P2Y <sub>12</sub> inhibitor (Prasugrel or Ticagrelor)
LEGACY (3000 pts)	DES	NSTEMI-ACS	No DAPT	P2Y <sub>12</sub> inhibitor (Prasugrel or Ticagrelor)

# De-escalation by Discontinuation: ASA or P2Y12i

19 Randomized Studies Comparing Antiplatelet Therapies After DAPT, N = 73,126



# Conclusions

## De-escalating by Discontinuation

---

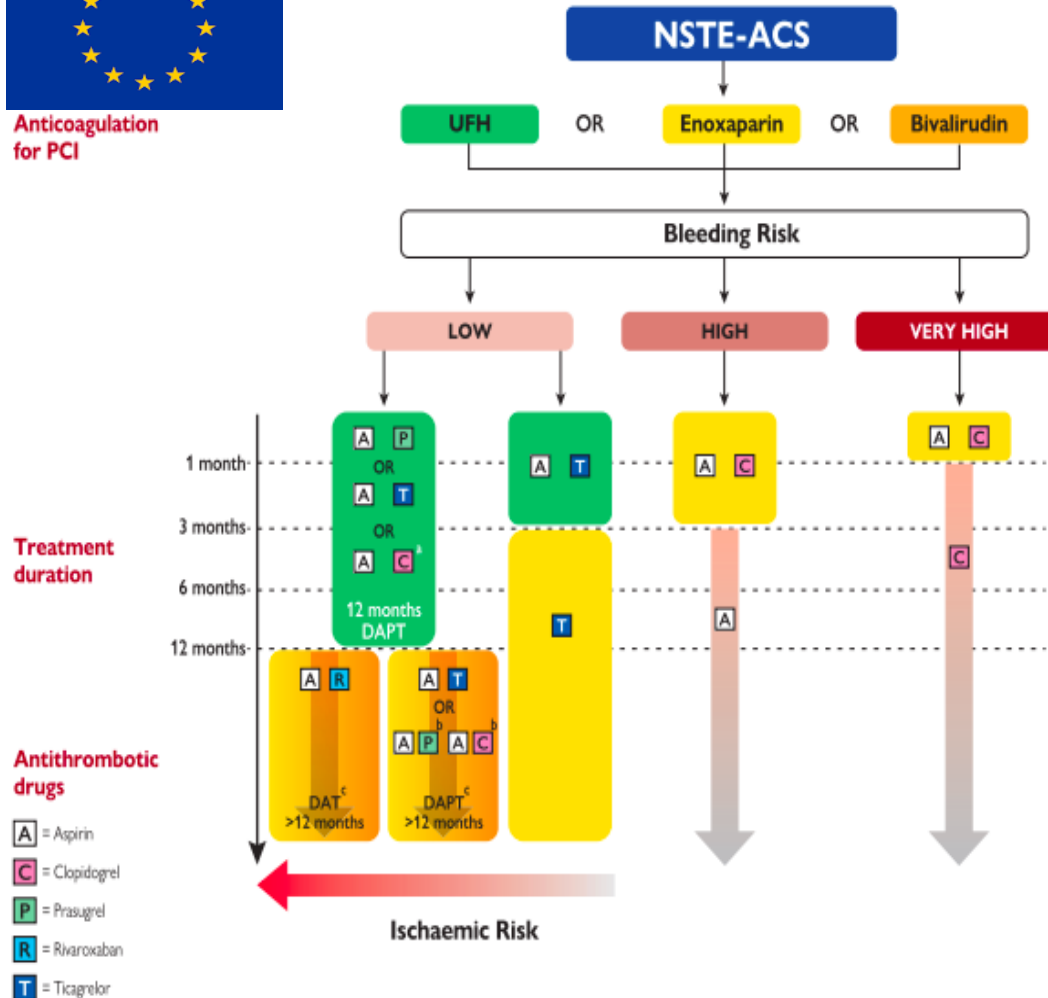
- ❖ De-escalating by discontinuation consist of stopping an antiplatelet drug with the intention to decrease the antiplatelet inhibitory effect
  
- ❖ Consensus that stopping P2Y12i or ASA is currently still based on physician discretion
  
- ❖ More data is needed on:
  - the impact and timing of P2Y12 inhibitor or ASA discontinuation in CCS and ACS;
  - the comparative effectiveness and safety of P2Y12 inhibitor or ASA discontinuation leading to SAPT;
  - the best SAPT strategy for chronic management beyond the 1- to 2- year period investigated in trials of P2Y12 inhibitor or ASA monotherapy.



# Current EU/US guidelines recommendations for Discontinuation<sup>1,2</sup>



Anticoagulation for PCI



The 2021 ACC/AHA/SCAI guidelines for coronary revascularization recommend that aspirin be discontinued at 1-3 months (class 2a), and the P2Y<sub>12</sub> inhibitor continued, regardless of bleeding risk and clinical presentation with ACS or CCS<sup>2</sup>.

1. Collet et al. 2020 ESC Guidelines for the management of NSTEMI. Eur Heart J 2021;42:1289–1367
2. Lawton et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization. Circulation 2021