

De-Escalation Strategy of Antithrombotic Therapy: Why, in Whom, and How?

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Disclosure Statement of Financial Interest

None

Antiplatelet Considerations



Both ischemic and bleeding events increases the risk of mortality!

DAPT Considerations

P2Y12 Potency

Ischemic Events



Potent P2Y12
(Prasugrel/Ticagrelor)



VS.

Bleeding Events



Less Potent P2Y12

- Clopidogrel
- Reduced dose P2Y12
Prasugrel (5 mg) or
Ticag (60 mg bid)

DAPT Considerations

Duration

Ischemic Events



Longer DAPT

VS.

Bleeding Events

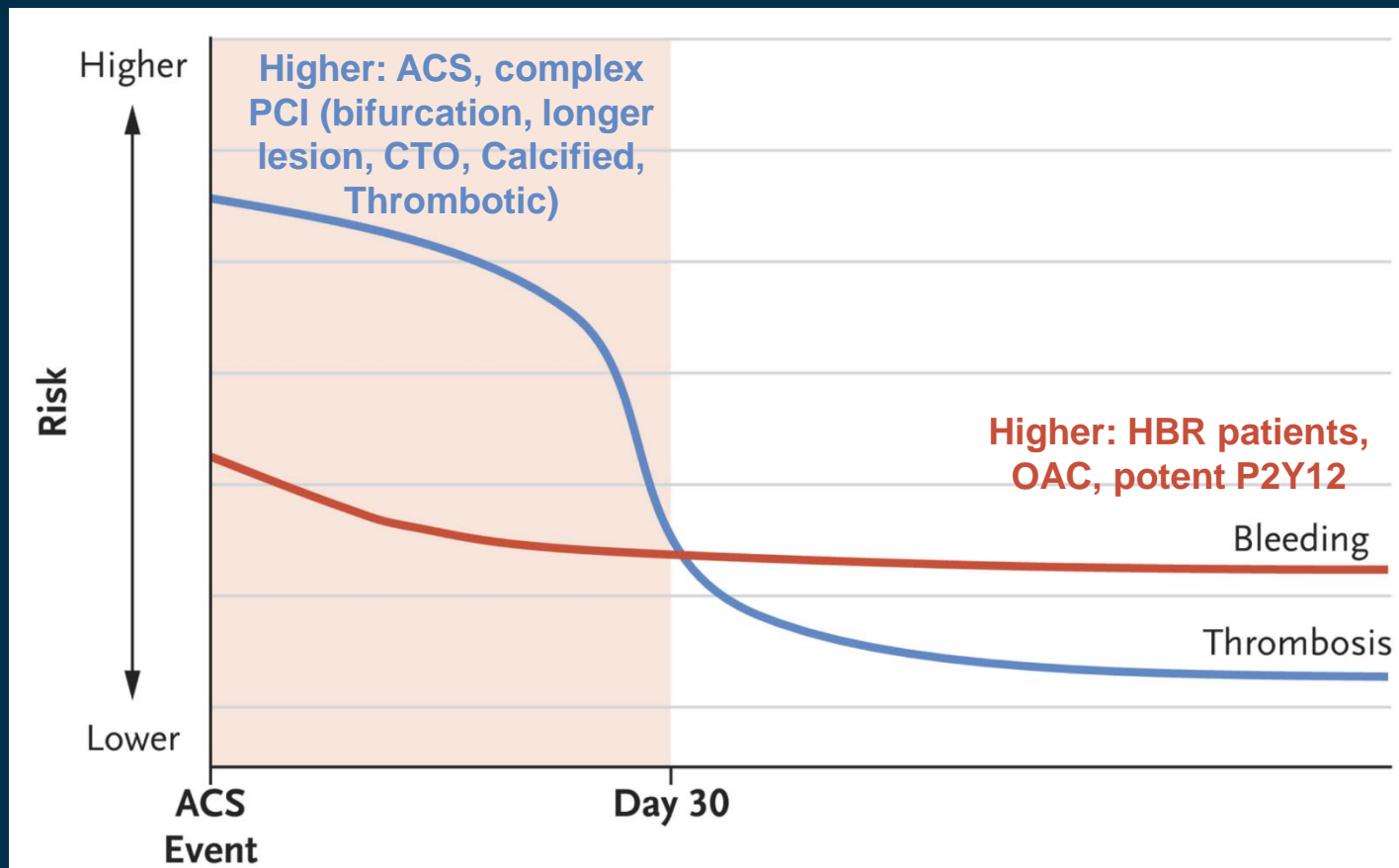


Shorter DAPT

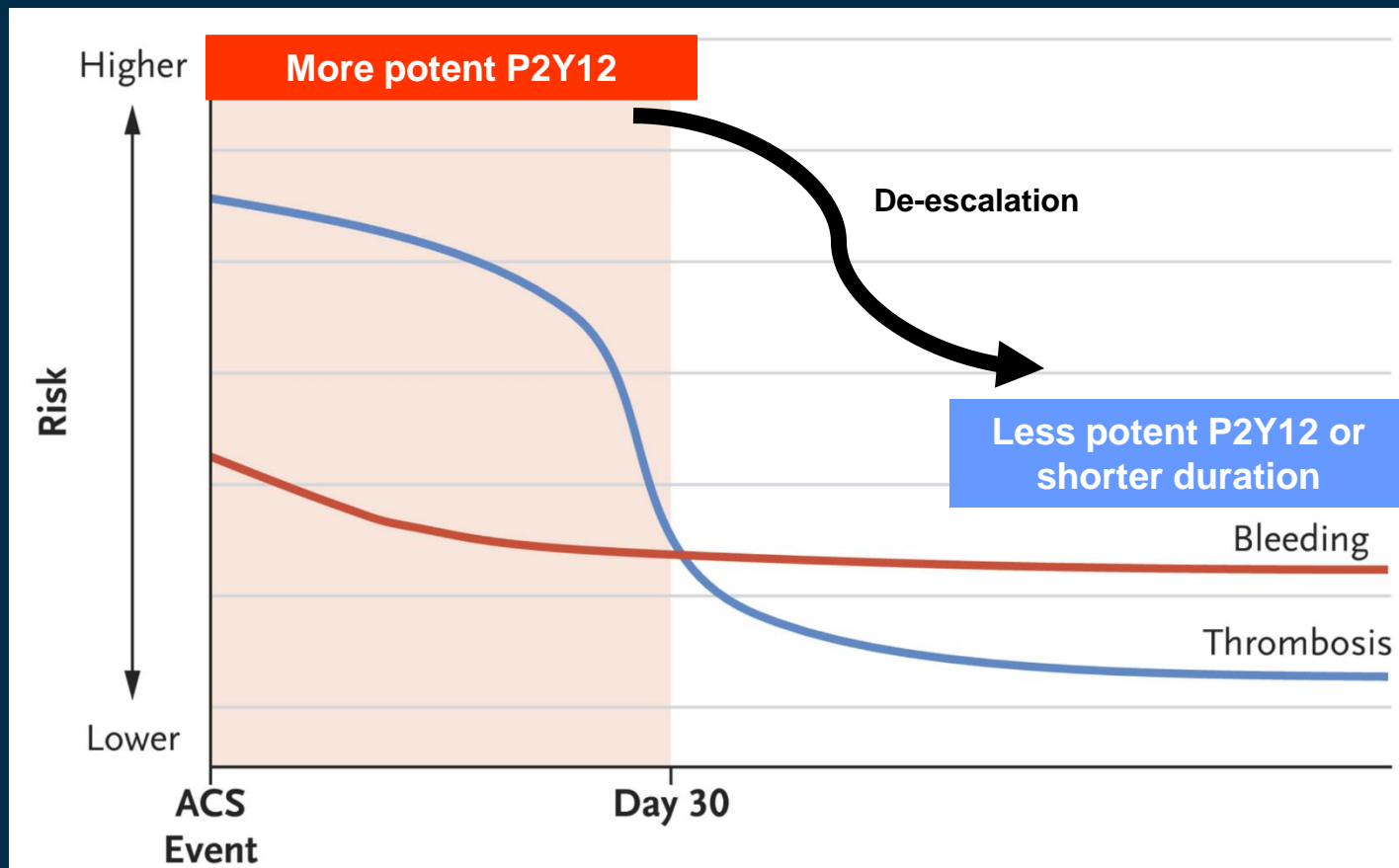
- Continue ASA
- Continue P2Y12

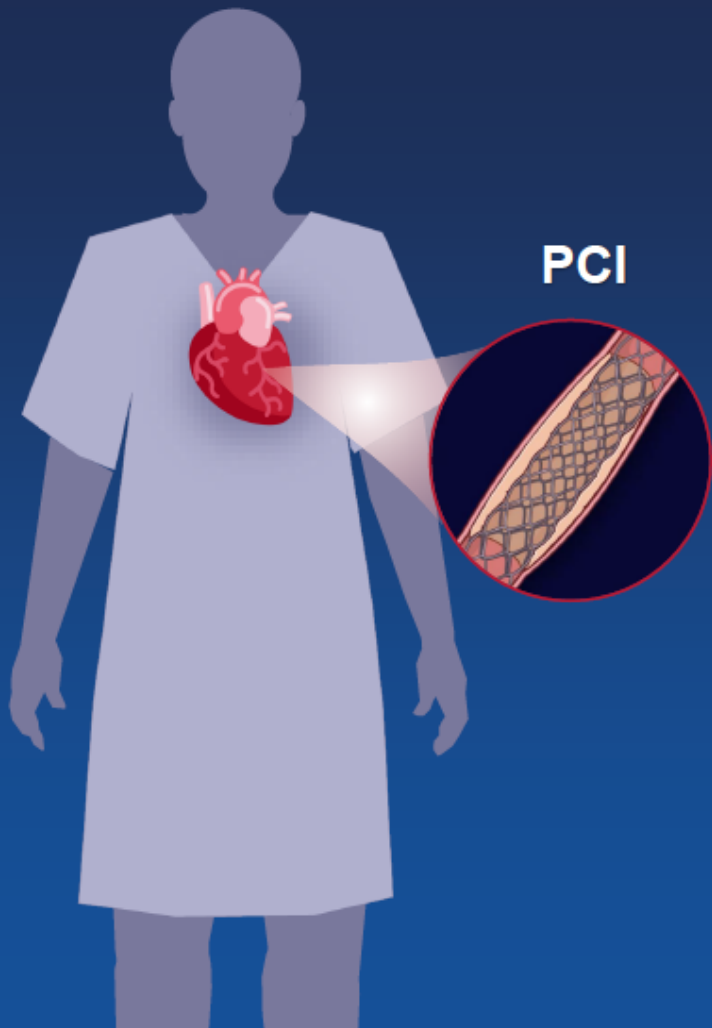


Timeline of Ischemic vs. Bleeding Risk after ACS



Timeline of Ischemic vs. Bleeding Risk after ACS





PCI

De-Escalation Strategies ARC Definition



Switch



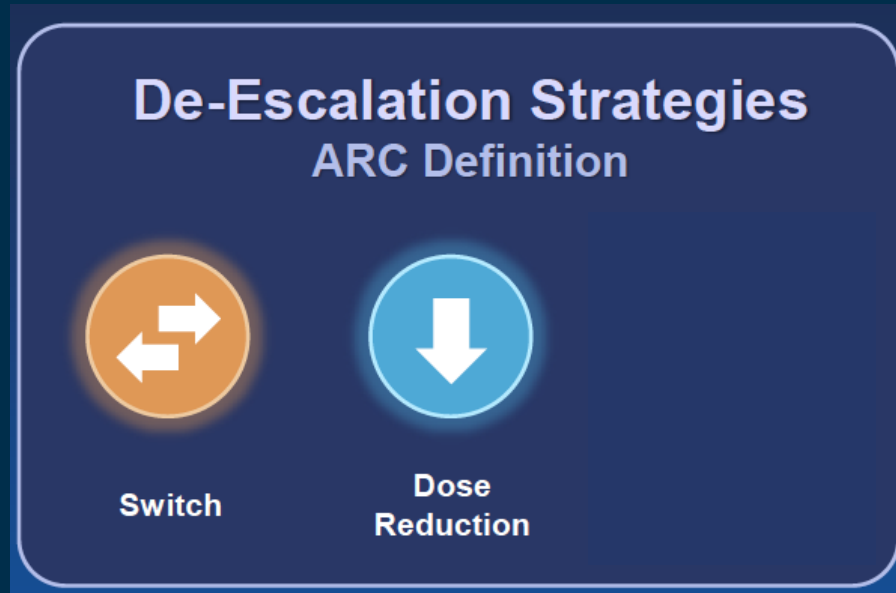
Dose
Reduction



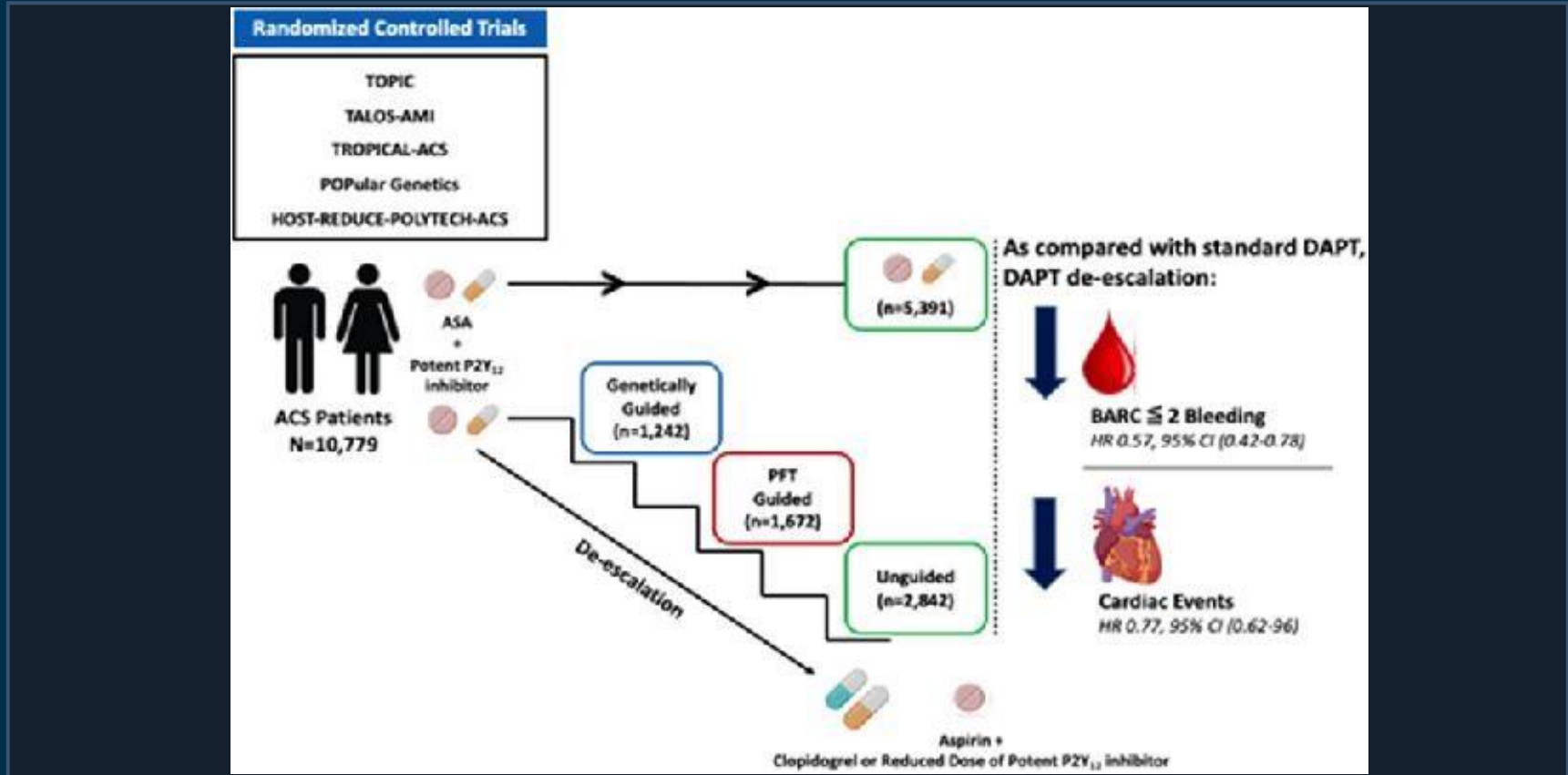
Discontinuation

De-escalation to less potent P2Y12 vs. Standard Potent DAPT

Why?



De-escalation from Potent P2Y12





TALOS-AMI

De-escalation at 30 days to unguided no loading clopidogrel

- 2697 patients (**STEMI 54%**; NSTEMI 46%) randomized after 1 month of ASA+Ticag
 - Group 1: ASA+Ticag for 11 months
 - Group 2: ASA+Clopidogrel for 11 months
- De-escalation resulted in
 - Reduced **NACE**- 45% ($P_{\text{sup}}=0.0001$)
 - Reduced **bleeding**- 48% ($P=0.0012$)
 - No difference in CV death, MI, stroke (2.1% vs. 3.1%; $P=0.15$)



TOPIC

De-escalation at 30 days to unguided no loading clopidogrel

- 646 patients (**STEMI 40%**; UA/NSTEMI 60%)
randomization after 1 month of ASA+Ticag/Prasugrel
 - Group 1: ASA+Ticag/Prasugrel for 11 months
 - Group 2: ASA+Clopidogrel (FDC) for 11 months
- De-escalation resulted in
 - Reduced **NACE**- 52% ($P_{\text{sup}} < 0.01$)
 - Reduced **bleeding**- 70% ($P < 0.01$)
 - No difference in ischemic endpoint (9.3% vs. 11.5%; $P = 0.36$)

De-escalation to shorter DAPT vs. Standard Potent DAPT

Why?

De-Escalation Strategies
ARC Definition



Discontinuation



TWILIGHT ACS: 3m vs. 12m DAPT

Short DAPT at 90 days by dropping ASA

- 4,614 patients at high bleeding or ischemic risk randomized to 3m DAPT (followed by Ticagrelor) vs. 12m DAPT (ASA+Ticagrelor)
- **STEMI: Excluded**, NSTEMI-ACS: 100%
- 3m when compared with 12m DAPT
 - **Reduced** bleeding ($p < 0.001$)
 - **No difference** for MI (3.1% vs. 3.1% ($p = 0.99$))
 - **No difference** in stent thrombosis (0.4% vs. 0.6% ($p = 0.38$))



STOPDAPT-2 ACS: 1m vs. 12m DAPT

Short DAPT at 30 days by dropping ASA

- 4,169 patients randomized to 1m DAPT (followed by clopidogrel) vs. 12 m DAPT
- **STEMI: 56%**, NSTEMI: 20%, and unstable angina: 24%
- 1m when compared with 12m DAPT
 - **Not Non-inferior** for NACE (CV death, MI, stroke, ST, TIMI major or minor bleeding)
 - **Increased** MI: 1.6% vs. 0.9% ($p < 0.05$)
 - **Reduced** bleeding



T-PASS: <1m vs. 12m DAPT

Short DAPT at 30 days by dropping ASA

- 2830 patients randomized to <1m DAPT (followed by Ticagrelor) vs. 12 m DAPT (ASA+Ticagrelor)
- **STEMI: 40%**, NSTEMI: 35%, and unstable angina: 24%
- <1m when compared with 12m DAPT
 - **Reduced NACE:** HR 0.54 (95% CI 0.37–0.80); $P_{NI} < 0.0001$; $P_{sup} = 0.002$
 - No difference in MACE: HR 0.84 (95% CI 0.50–1.41); $P = 0.51$
 - MI: 0.5% vs. 0.6%; $P = 0.80$
 - **Reduced bleeding:** HR 0.35 (95% CI 0.20–0.61); $P < 0.0001$



ULTIMATE-DAPT: 1m vs. 12m DAPT

Short DAPT at 30 days by dropping ASA

- 3400 patients randomized to 1m DAPT (followed by Ticagrelor) vs. 12 m DAPT (ASA+Ticagrelor)
- **STEMI: 28%**, NSTEMI: 32%, and unstable angina: 40%
- 1m when compared with 12m DAPT
 - **Reduced NACE:** HR 0.45 (0.30 to 0.66); $P < 0.0001$
 - No difference in MACE: HR 0.98 (0.69 to 1.39); $P_{NI} < 0.0001$
 - MI: 0.9% vs. 0.7%; $P = 0.29$
 - **Reduced bleeding:** HR 0.68 (0.53 – 0.88); $P = 0.007$



STOP DAPT-3: 0m vs. 12m DAPT

P2Y12 Monotherapy vs. DAPT

- 5966 patients randomized to 0m DAPT (Prasugrel 3.75 mg) vs. 12 m DAPT (ASA+Prasugrel 3.75 mg)
- **STEMI: 43%**
- 0m when compared with 12m DAPT
 - No difference in bleeding: HR 0.95, 0.75-1.20; P= 0.66
 - No difference in MACE (30 days): HR 1.12, CI 0.87-1.45; $P_{NI} = 0.01$
 - **Increase in subacute ST:** HR 3.40, 95% CI 1.26-9.23; $p < 0.05$

De-escalation to shorter DAPT vs. De-escalation to less potent P2Y12

Why?

De-Escalation Strategies ARC Definition



Switch



Dose
Reduction

VS

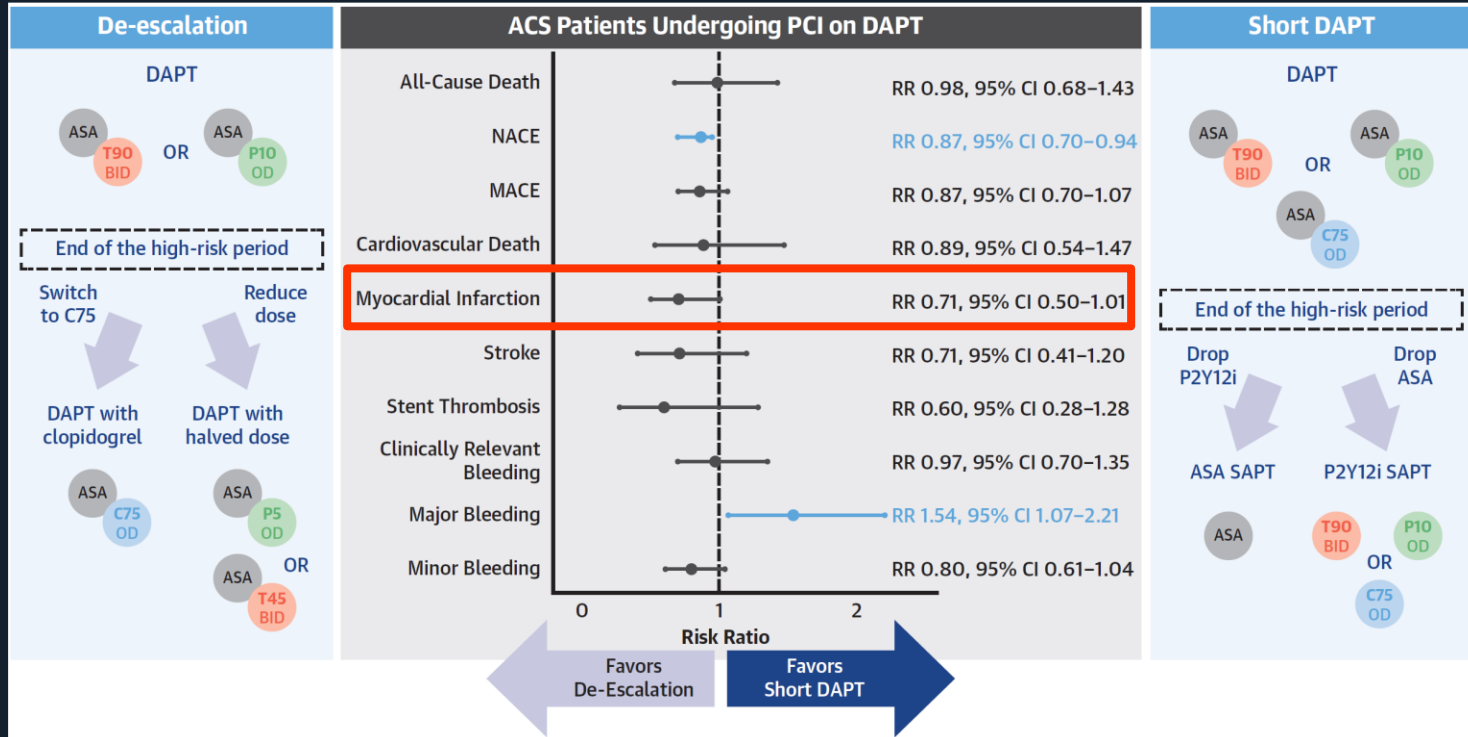
De-Escalation Strategies ARC Definition



Discontinuation

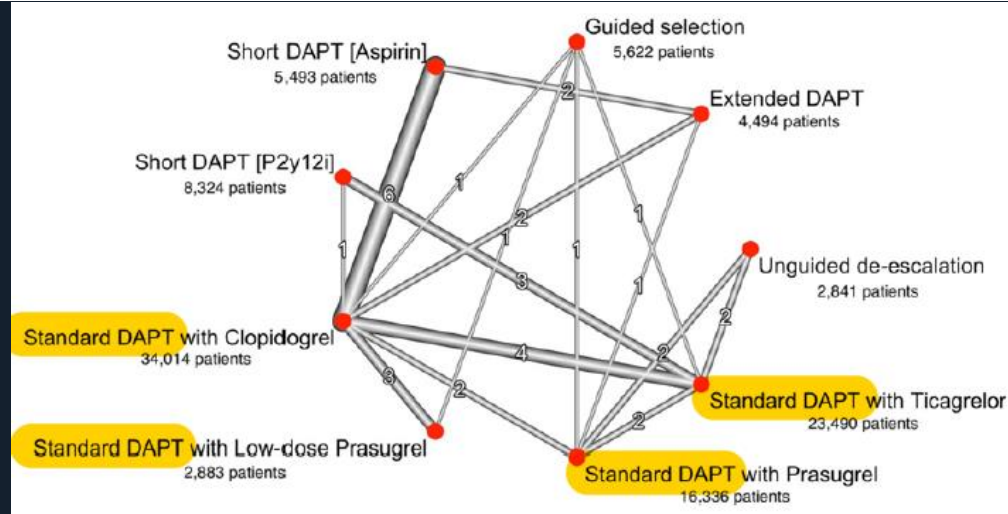
ACS Patients

De-escalation vs. Short DAPT strategy



Short-Term DAPT and DAPT De-Escalation Strategies for Patients With Acute Coronary Syndromes: A Systematic Review and Network Meta-Analysis

Toshiki Kuno¹, MD, PhD; Atsuyuki Watanabe², MD; Satoshi Shoji, MD, PhD; Tomohiro Fujisaki³, MD; Hiroki Ueyama, MD; Hisato Takagi⁴, MD, PhD; Pierre Deharo⁵, MD; Thomas Cuisset, MD; Sripal Bangalore⁶, MD, MHA; Roxana Mehran⁷, MD; Gregg W. Stone⁸, MD; Shun Kohsaka⁹, MD, PhD*; Deepak L. Bhatt¹⁰, MD, MPH*



DAPT strategies in ACS: Ranking

- **MACE**
 1. Unguided de-es
 2. Guided selection
- **MI**
 1. Extended DAPT
 2. Guided selection
- **Bleeding**
 1. Unguided de-es
 2. Short DAPT (P₂Y₁₂)
- **Death**
 1. Short DAPT (P₂Y₁₂)
 2. Unguided de-es
- **Stroke**
 1. Guided selection
 2. Extended DAPT
- **CV death**
 1. Unguided de-es
 2. Short DAPT (P₂Y₁₂)
- **Stent thrombosis**
 1. Extended DAPT
 2. Std DAPT w low P

De-escalation vs. Standard Potent DAPT

How and When?

De-escalation Strategies in ACS

Genetically guided

PFT guided

Unguided

**Genetic testing post
PCI (point of care vs.
central lab)**

De-escalation Strategies in ACS

Genetically guided

PFT guided

Unguided



De-escalation Strategies in ACS

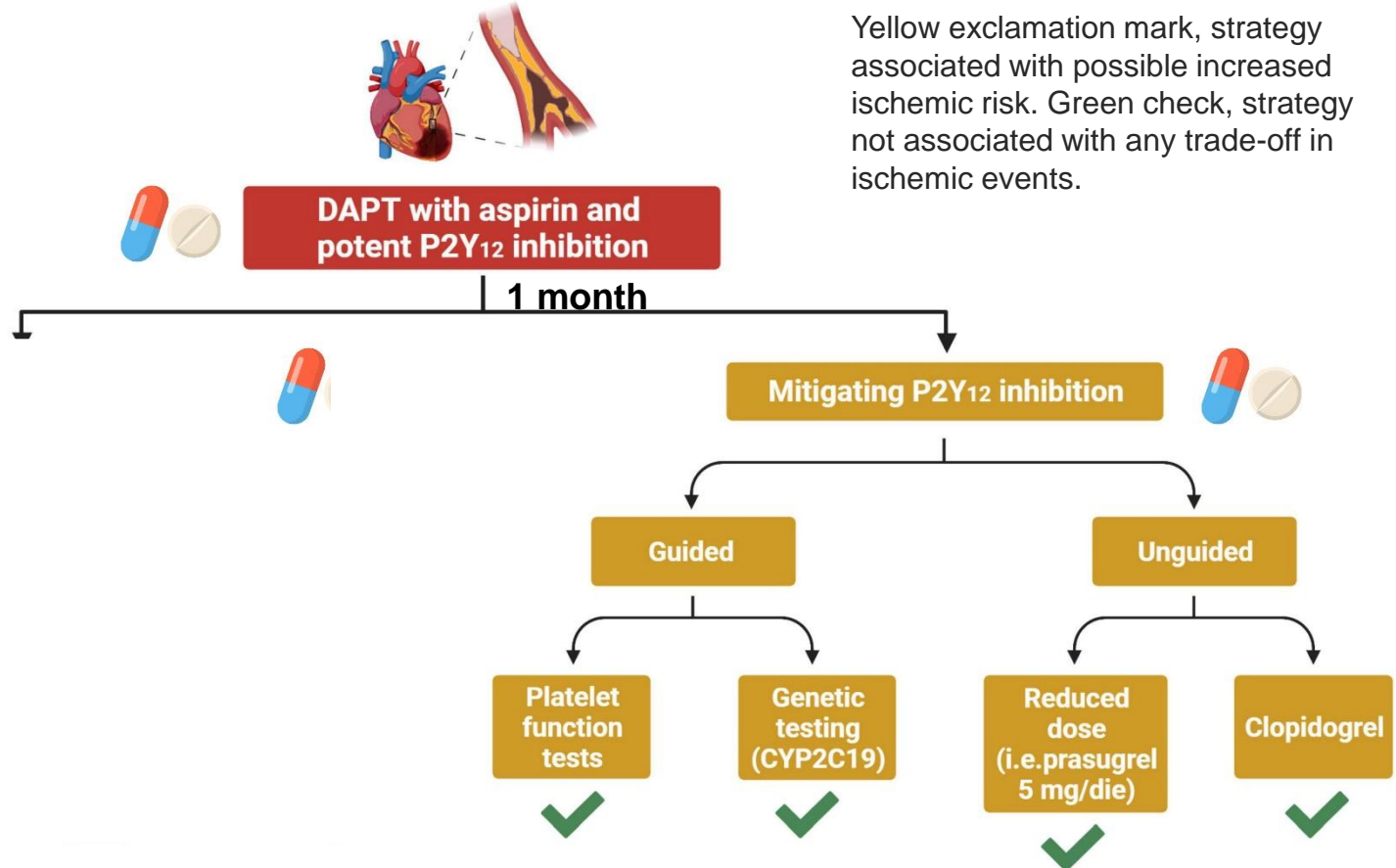
Genetically guided

PFT guided

Unguided

No loading and no testing

De-escalation Strategies in ACS: Summary





IT'S ALL ABOUT THE BALANCE