



# **HOT TOPICS IN CARDIOLOGIA 2024**

**27 e 28 Novembre 2024**

Villa Doria D'Angri - Via F. Petrarca 80,  
Napoli

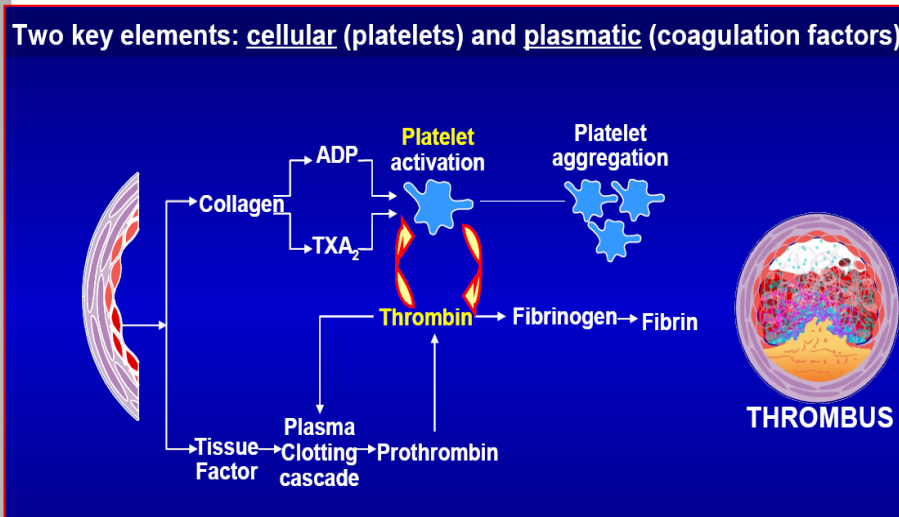
## **De-escalation o short DAPT: cosa, a chi?**

**Plinio Cirillo,  
Università di Napoli  
«Federico II»**

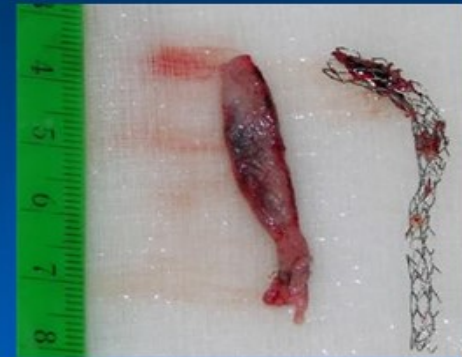
# DAPT after ACS Rationale

## ACS pathophysiology

Two key elements: cellular (platelets) and plasmatic (coagulation factors)



## Stent Thrombosis



Platelet-mediated events.

## 2023 ESC Guidelines for the management of acute coronary syndromes

Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC)

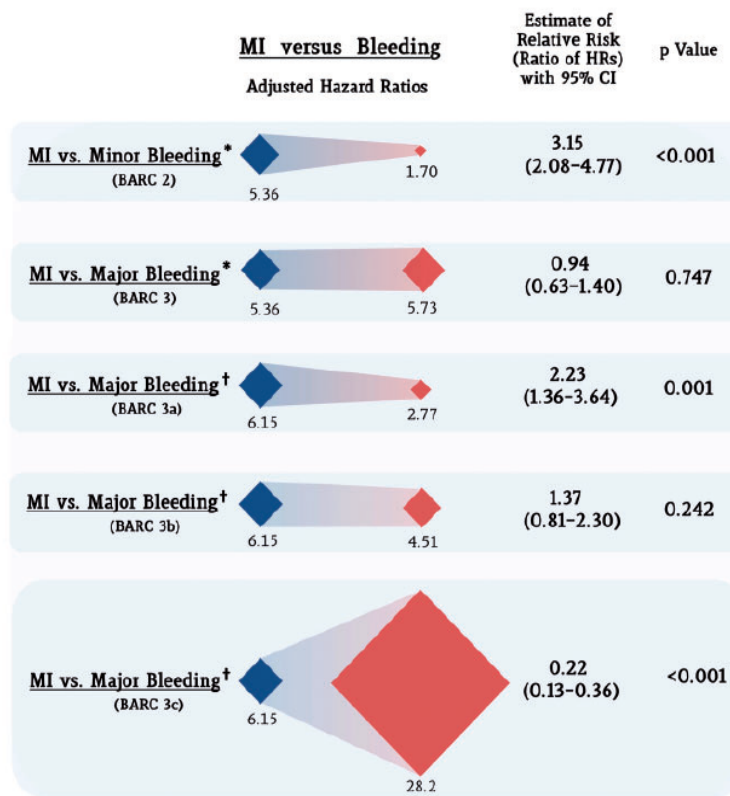
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<b>Antiplatelet therapy</b>		
Aspirin is recommended for all patients without contraindications at an initial oral LD of 150–300 mg (or 75–250 mg i.v.) and an MD of 75–100 mg o.d. for long-term treatment. <a href="#">284,285</a>	I	A
In all ACS patients, a P2Y <sub>12</sub> receptor inhibitor is recommended in addition to aspirin, given as an initial oral LD followed by an MD for 12 months	I	A

# Trade-off of myocardial infarction vs. bleeding types on mortality after acute coronary syndrome: lessons from the Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome (TRACER) randomized trial

Marco Valgimigli<sup>1,2\*</sup>, Francesco Costa<sup>2,3</sup>, Yuliya Lokhnygina<sup>4</sup>, Robert M. Clare<sup>4</sup>, Lars Wallentin<sup>5</sup>, David J. Moliterno<sup>6</sup>, Paul W. Armstrong<sup>7</sup>, Harvey D. White<sup>8</sup>, Claes Held<sup>5</sup>, Philip E. Aylward<sup>9</sup>, Frans Van de Werf<sup>10</sup>, Robert A. Harrington<sup>11</sup>, Kenneth W. Mahaffey<sup>11</sup>, and Pierluigi Tricoci<sup>4</sup>

## BLEEDING IMPACTS ON MORTALITY!!!

12 944 patients with non-ST-segment elevation ACS

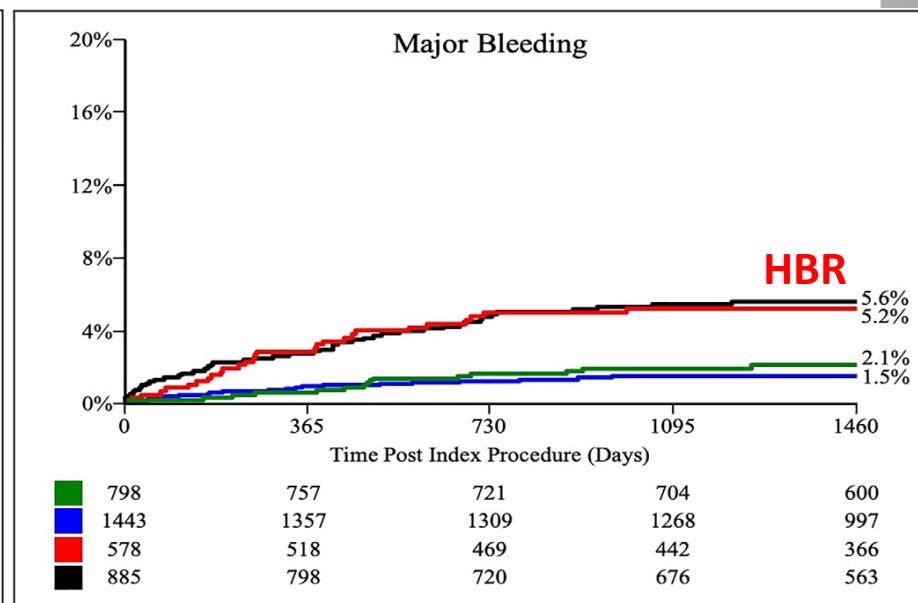
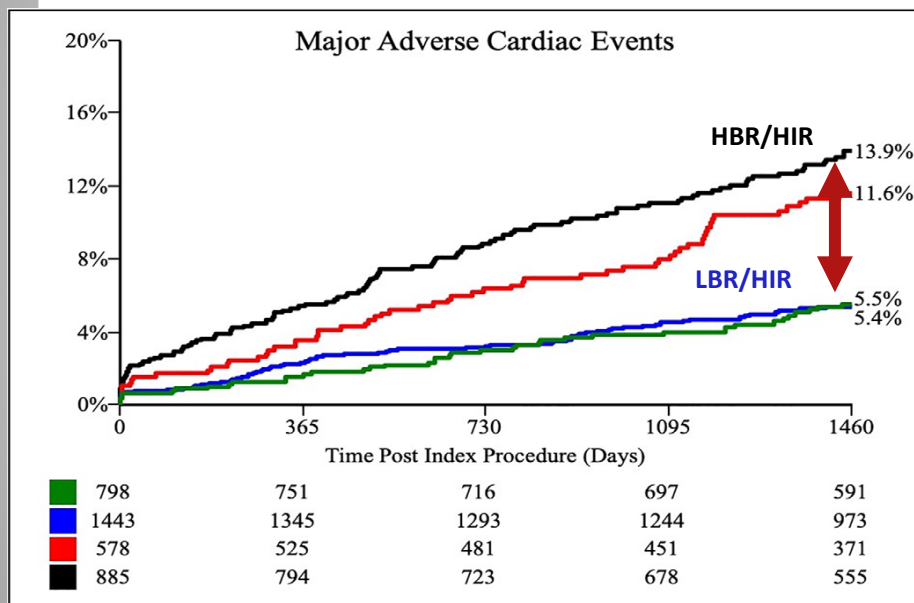


**Figure 2** Differential impact of myocardial infarction vs. bleeding on mortality. Blue rhombuses represent the magnitude (adjusted hazard ratio) of the impact on mortality of late myocardial infarction, whereas red rhombuses represent that of bleeding of different severity. On the right part of the figure, the estimate of the relative risk (ratio of the hazard ratios) for each category is presented. \*The estimates of the impact of events on mortality is derived from Model 1, including BARC 3 bleeding as a single category. †The estimates of the impact of events on mortality is derived from Model 2, including BARC 3 bleeding subcategories separately. MI, myocardial infarction.

# Comparative influence of bleeding and ischemic risk factors on diabetic patients undergoing percutaneous coronary intervention with everolimus-eluting stents

Ridhima Goel MD<sup>1</sup> | Davide Cao MD<sup>1,2</sup> | Rishi Chandiramani MD<sup>1</sup> | Anastasios Roumeliotis MD<sup>1</sup> | Moritz Blum BS<sup>1</sup> | Deepak L. Bhatt MD, MPH<sup>3</sup> | Dominick J. Angiolillo MD, PhD<sup>4</sup> | Junbo Ge MD<sup>5</sup> | Ashok Seth MD, FRCP, DSc<sup>6</sup> | Shigeru Saito MD<sup>7</sup> | Mitchell Krucoff MD<sup>8</sup> | Ken Kozuma MD, PhD<sup>9</sup> | Rajendra M. Makkar MD<sup>10</sup> | Sripal Bangalore MD, MHA<sup>11</sup> | Lijuan Wang PhD<sup>12</sup> | Kai Koo PhD<sup>12</sup> | Franz-Josef Neumann MD<sup>13</sup> | James Hermiller MD<sup>14</sup> | Giulio Stefanini MD, PhD<sup>2</sup> | Marco Valgimigli MD, PhD<sup>15</sup> | Roxana Mehran MD<sup>1</sup>

3,704 DM patients were divided into four groups



Low bleeding risk  
Low ischemic risk

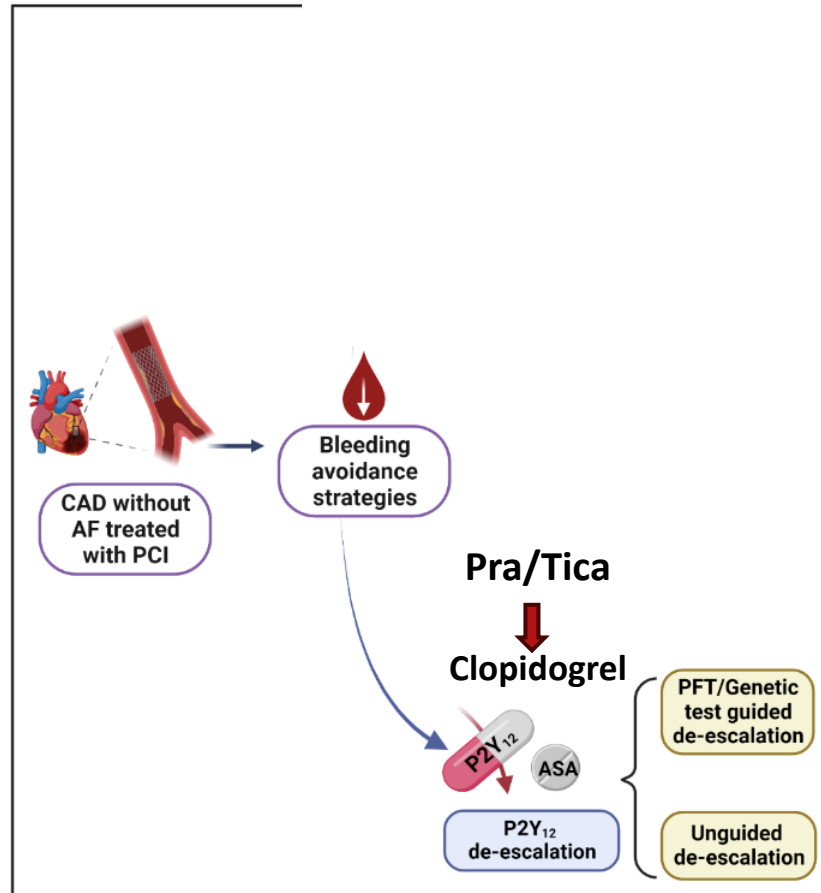
Low bleeding risk  
High ischemic risk

High bleeding risk  
Low ischemic risk

High bleeding risk  
High ischemic risk

Catheter Cardiovasc Interv. 2021;98:1111–1119.

# Hypothetical strategies to reduce bleeding



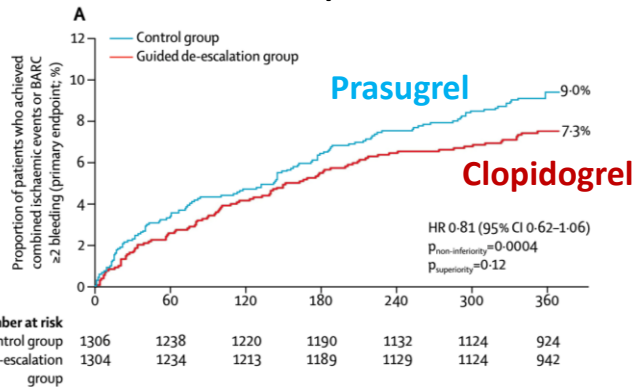
Adapted by Zhioue te al. J. Cardiovasc. Dev. Dis. 2022, 9, 340.

# Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial

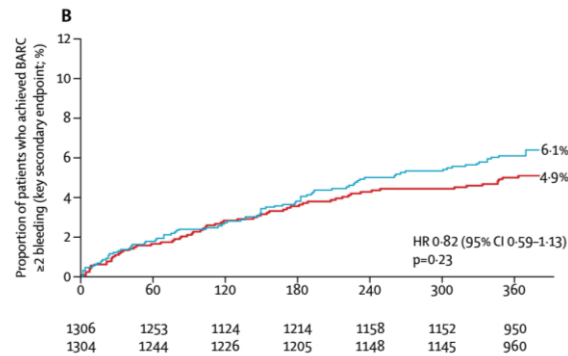
Dirk Sibbing\*, Dániel Aradi\*, Claudius Jacobshagen, Lisa Gross, Dietmar Trenk, Tobias Geisler, Martin Orban, Martin Hadamitzky, Béla Merkely, Róbert Gábor Kiss, András Komócsi, Csaba A Dézsi, Lesca Holdt, Stephan B Felix, Radoslaw Parma, Mariusz Klopotoski, Robert H G Schwinger, Johannes Rieber, Kurt Huber, Franz-Josef Neumann, Lukasz Koltowski, Julinda Mehilli, Zenon Huczek, Steffen Massberg, on behalf of the TROPICAL-ACS Investigators†

2610 eligible patients with acute coronary syndrome

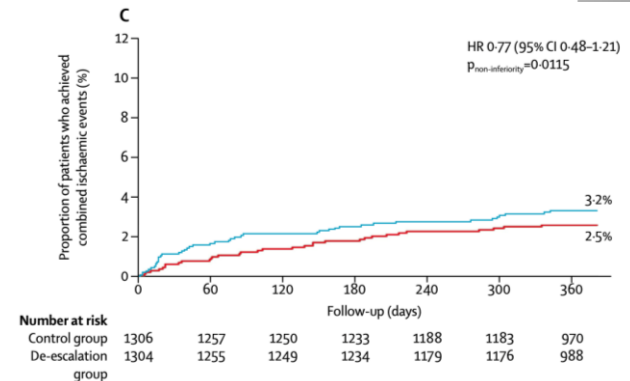
## Combined ischemic/BARC >2 events



## BARC > 2 events



## Ischemic events

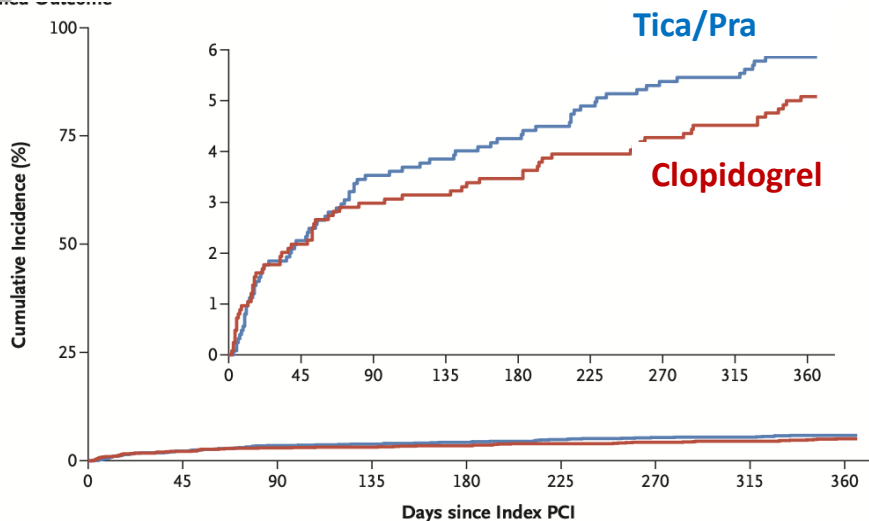


Lancet 2017; 390: 1747-57

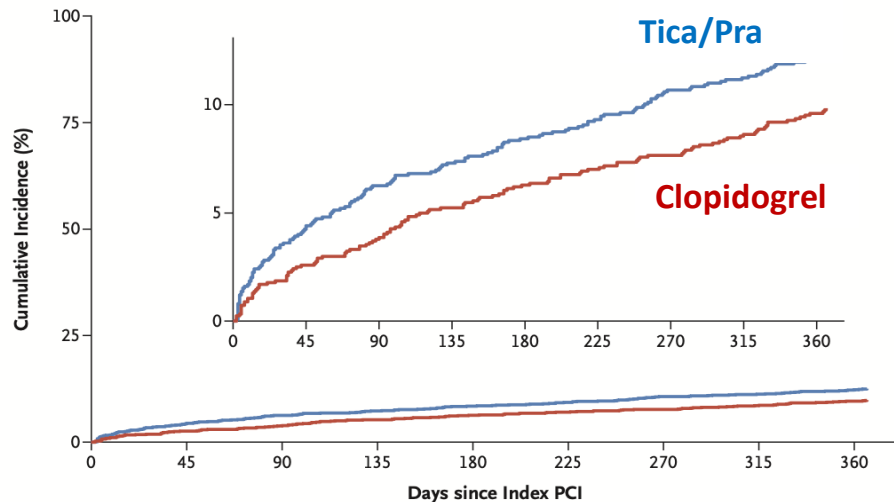
## A Genotype-Guided Strategy for Oral P2Y<sub>12</sub> Inhibitors in Primary PCI

Daniel M.F. Claassens, M.D., Gerrit J.A. Vos, M.D., Thomas O. Bergmeijer, M.D., Renicus S. Hermanides, M.D., Ph.D., Arnoud W.J. van 't Hof, M.D., Ph.D., Pim van der Harst, M.D., Ph.D., Emanuele Barbato, M.D., Ph.D., Carmine Morisco, M.D., Ph.D., Richard M. Tjon Joe Gin, M.D., Folkert W. Asselbergs, M.D., Ph.D., Arend Mosterd, M.D., Ph.D., Jean-Paul R. Herrman, M.D., Ph.D., Willem J.M. Dewilde, M.D., Ph.D., Paul W.A. Janssen, M.D., Ph.D., Johannes C. Kelder, M.D., Ph.D., Maarten J. Postma, Ph.D., Anthonius de Boer, M.D., Ph.D., Cornelis Boersma, Pharm.D., Ph.D., Vera H.M. Deneer, Pharm.D., Ph.D., and Jurriën M. ten Berg, M.D., Ph.D.

2488 patients were included primary PCI with stent implantation



death for any cause, MI, stent thrombosis, stroke and major bleeding



Major Bleeding

N ENGL J MED 2019: 381; 17: OCTOBER 24



Unguided de-escalation from ticagrelor to clopidogrel in stabilised patients with acute myocardial infarction undergoing percutaneous coronary intervention (TALOS-AMI): an investigator-initiated, open-label, multicentre, non-inferiority, randomised trial

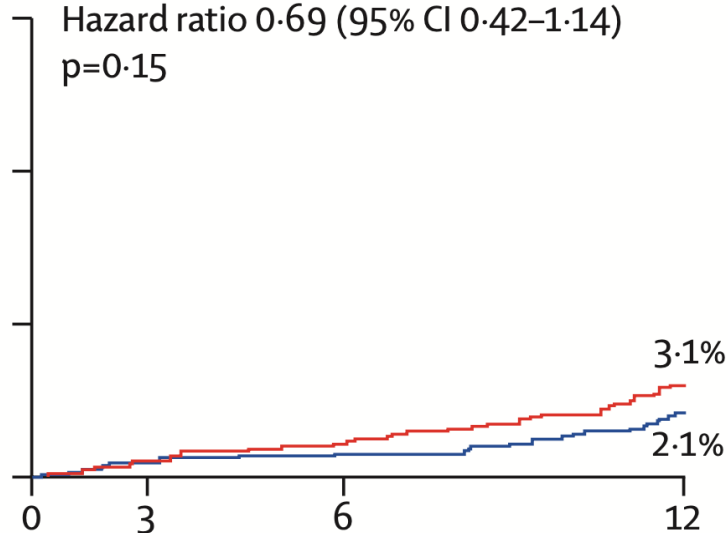


Chan Joon Kim\*, Mahn-Won Park\*, Min Chul Kim, Eun-Ho Choo, Byung-Hee Hwang, Kwan Yong Lee, Yun Seok Choi, Hee-Yeol Kim, Ki-Dong Yoo, Doo-Soo Jeon, Eun-Seok Shin, Young-Hoon Jeong, Ki-Bae Seung, Myung Ho Jeong, Hyeon Woo Yim, Youngkeun Ahn, Kiyuk Chang, TALOS-AMI investigators†

2697 patients were randomly assigned:  
1349 patients to de-escalation and 1348 to active control groups.

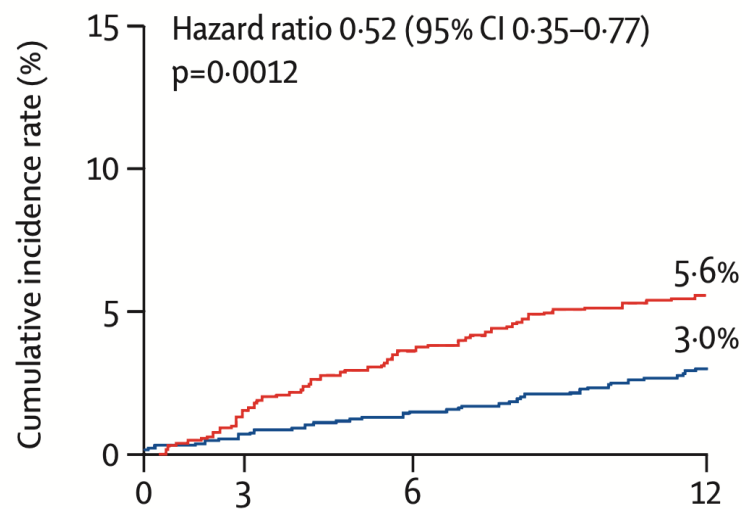
**B Composite of CV death, MI, or stroke**

Hazard ratio 0.69 (95% CI 0.42–1.14)  
p=0.15



**C Composite of BARC bleeding type 2, 3, or 5**

Hazard ratio 0.52 (95% CI 0.35–0.77)  
p=0.0012



TALOS-AMI. Lancet 2021; 398: 1305–16

# Guided and unguided de-escalation from potent P2Y<sub>12</sub> inhibitors among patients with acute coronary syndrome: a meta-analysis

Anne H. Tavenier<sup>1,2</sup>, Roxana Mehran<sup>1</sup>, Mauro Chiarito<sup>1</sup>, Davide Cao<sup>1</sup>, Carlo A. Pivato<sup>1,3,4</sup>, Johnny Nicolas<sup>1</sup>, Frans Beerkens<sup>1</sup>, Matteo Nardin<sup>1</sup>, Samantha Sartori<sup>1</sup>, Usman Baber<sup>1</sup>, Dominick J. Angiolillo<sup>5</sup>, Davide Capodanno<sup>6</sup>, Marco Valgimigli<sup>7,8</sup>, Renicus S. Hermanides<sup>2</sup>, Arnaud W.J. van 't Hof<sup>2,9</sup>, Jur M. ten Berg<sup>9,10</sup>, Kiyuk Chang<sup>11</sup>, Annapoorna S. Kini<sup>1</sup>, Samin K. Sharma<sup>1</sup> and George Dangas<sup>1,\*</sup>

10 779 patients.

DAPT de-escalation (genetically or platelet function guided to clopidogrel; unguided to clopidogrel; unguided to lower dose vs. standard DAPT

## Bleeding events

## MACE

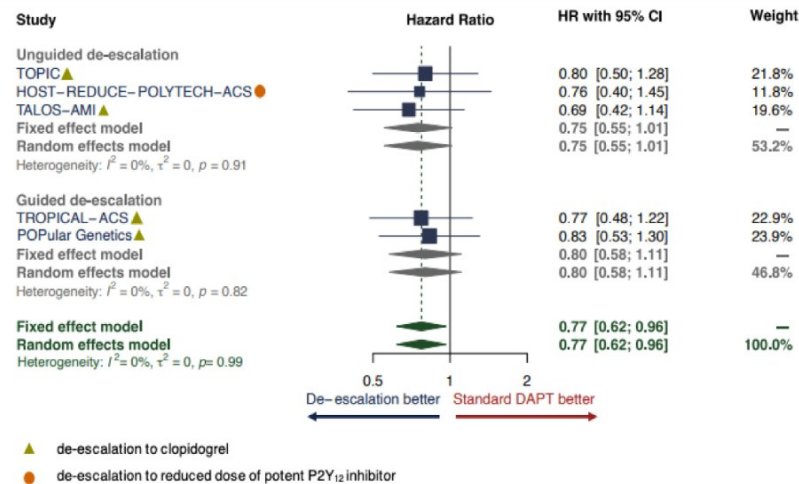
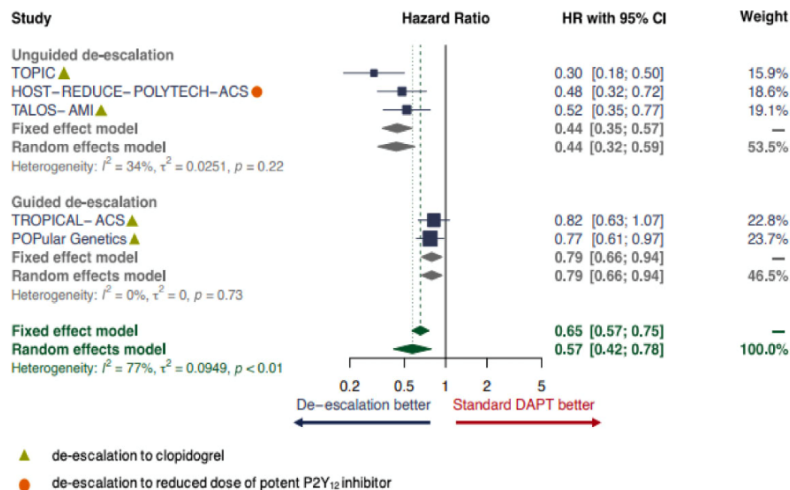


Figure 2 Forest plot comparing DAPT de-escalation to standard DAPT on clinically relevant bleeding events (BARC  $\geq 2$  bleeding).

Figure 3 Forest plot comparing DAPT de-escalation to standard DAPT on major adverse cardiac events.

## 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

**Recommendations**

**Class<sup>a</sup>**

**Level<sup>b</sup>**

### Shortening/de-escalation of antithrombotic therapy

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**



**ESC**

European Society of Cardiology

European Heart Journal (2023) 44, 3720–3826  
<https://doi.org/10.1093/eurheartj/ehad191>

**ESC GUIDELINES**

## 2023 ESC Guidelines for the management of acute coronary syndromes

Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC)

**Recommendations**

**Class<sup>a</sup>**

**Level<sup>b</sup>**

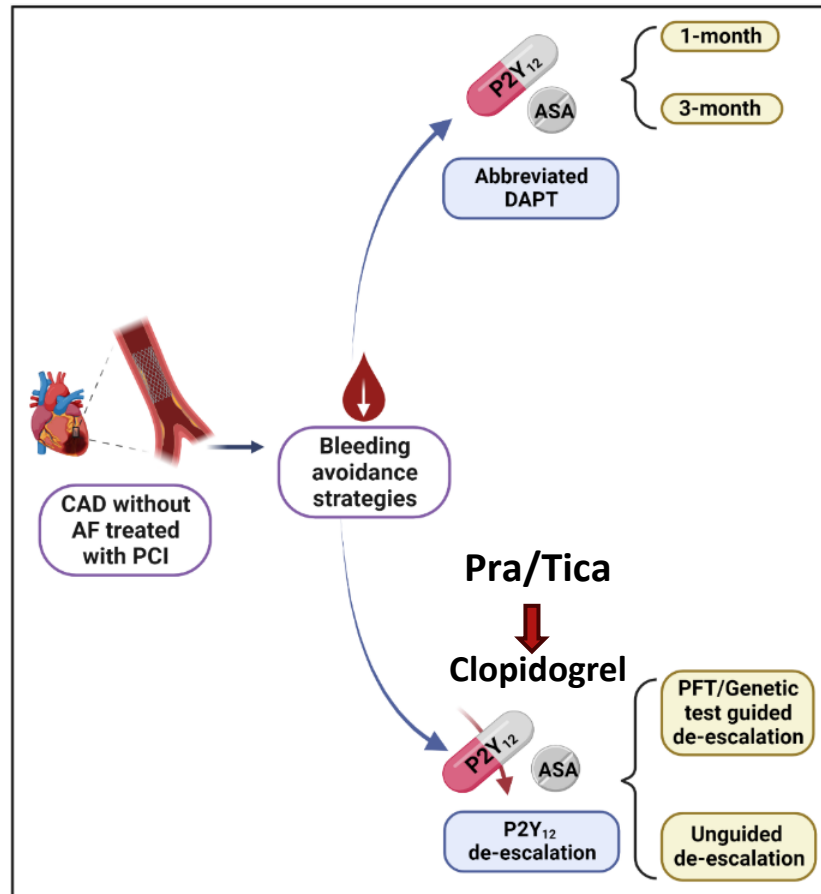
### Shortening/de-escalation of antithrombotic therapy

De-escalation of P2Y<sub>12</sub> receptor inhibitor treatment (e.g. with a switch from prasugrel/ticagrelor to clopidogrel) may be considered as an alternative DAPT strategy to reduce bleeding risk.<sup>279–282,321,322</sup>

**IIb**

**A**

# Hypothetical strategies to reduce bleeding



ASA  
Clopidogrel  
Ticagrelor  
Prasugrel

Adapted by Zhioue te al. J. Cardiovasc. Dev. Dis. 2022, 9, 340.

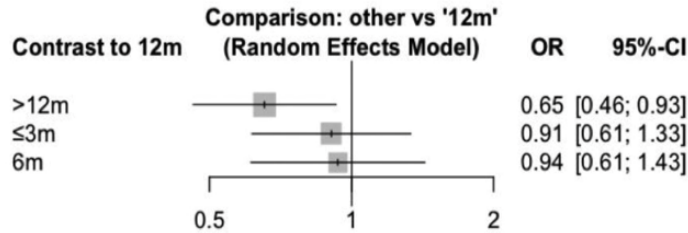
31,837 patients



Optimal Duration of Dual Antiplatelet Therapy After Percutaneous Coronary Intervention in Patients With Acute Coronary Syndrome: Insights From a Network Meta-Analysis of Randomized Trials

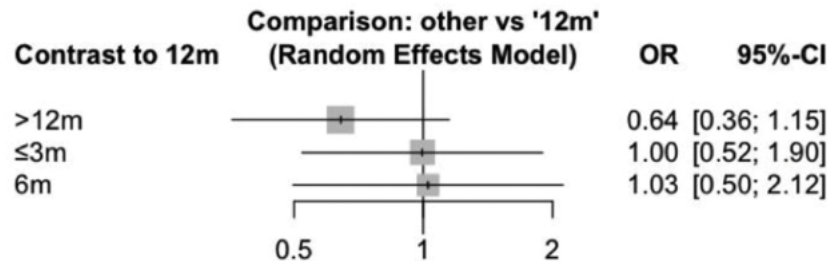


**≤3 months vs. 6 months vs. 12 months vs. >12 months**

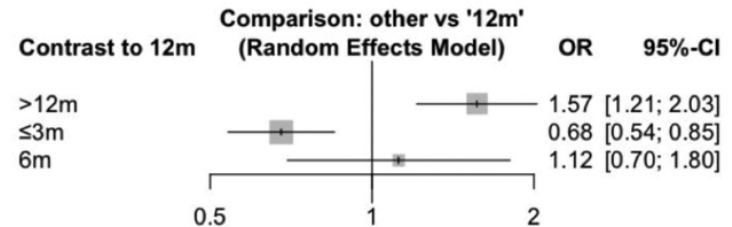


**Myocardial Infarction**

B



**Stent Thrombosis**



**BARC 3-5**

## 2023 ESC Guidelines for the management of acute coronary syndromes

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### Grading of short DAPT and de-escalation in GLs

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<b>Shortening/de-escalation of antithrombotic therapy</b>		
In patients who are event-free after 3–6 months of DAPT and who are on dual antiplatelet therapy, de-escalation to single antiplatelet therapy with a P2Y <sub>1</sub> receptor inhibitor may be considered as an alternative DAPT strategy to reduce bleeding risk. <a href="#">271,273,274,276,313</a>	Ib	A
De-escalation of DAPT (e.g. with a switch from prasugrel/tegragrelor to clopidogrel) may be considered as an alternative DAPT strategy to reduce bleeding risk. <a href="#">279–282,321,322</a>	IIb	A

**HBR: WHICH TIMING TO REDUCE DAPT??**

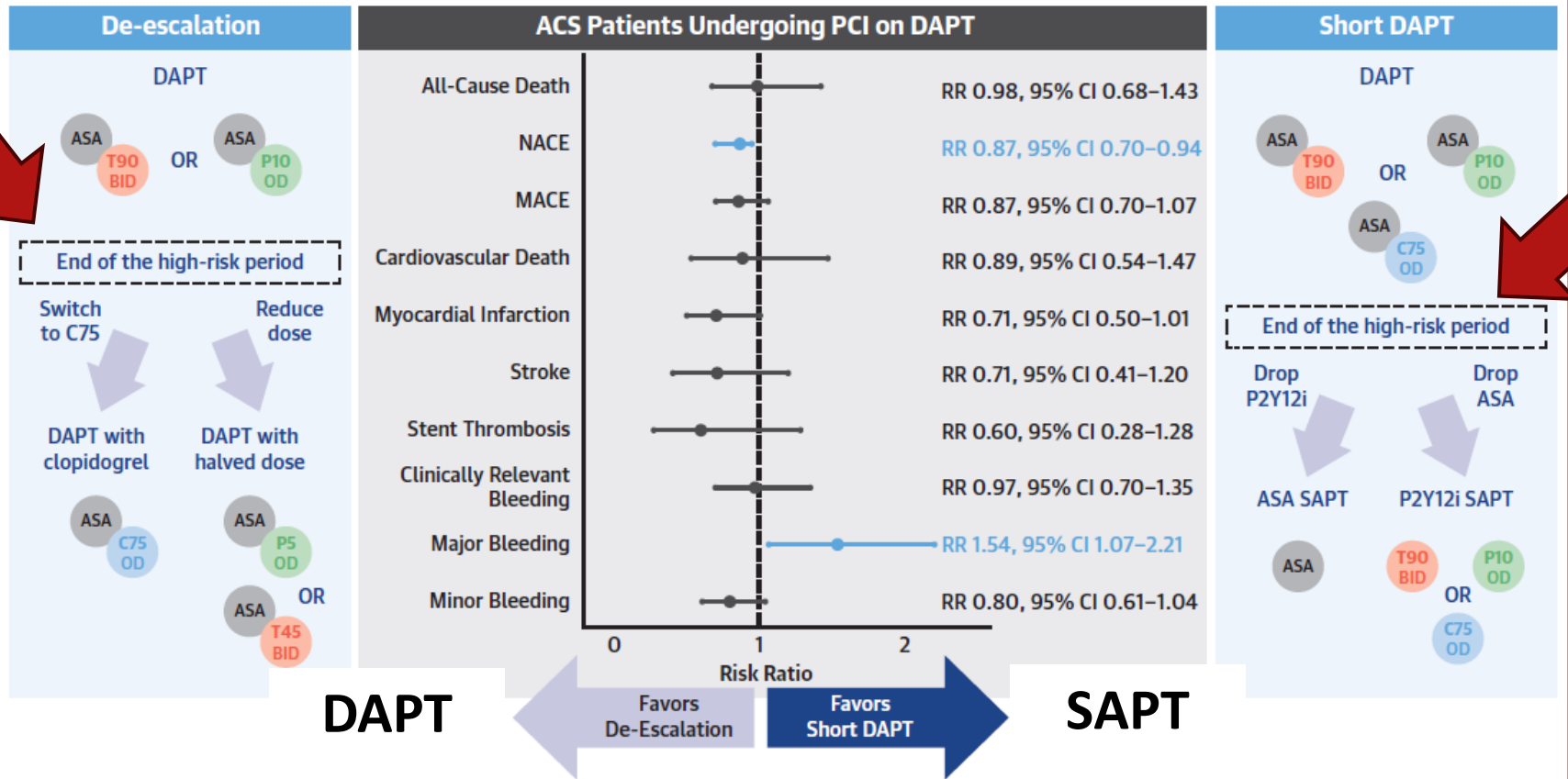
# Short Duration of DAPT Versus De-Escalation After Percutaneous Coronary Intervention for Acute Coronary Syndromes



Claudio Laudani, MD,<sup>a</sup> Antonio Greco, MD,<sup>a</sup> Giovanni Occhipinti, MD,<sup>a</sup> Salvatore Ingala, MD,<sup>a</sup> Dario Calderone, MD,<sup>a</sup> Lorenzo Scalia, MD,<sup>a</sup> Federica Agnello, MD,<sup>a</sup> Marco Legnazzi, MD,<sup>a</sup> Maria Sara Mauro, MD,<sup>a</sup> Carla Rochira, MD,<sup>a</sup> Sergio Buccheri, MD,<sup>b</sup> Roxana Mehran, MD,<sup>c</sup> Stefan James, MD,<sup>b</sup> Dominick J. Angiolillo, MD, PhD,<sup>d</sup> Davide Capodanno, MD, PhD<sup>e</sup>

J Am Coll Cardiol Intv. 2022;15(3):268-277.

## CENTRAL ILLUSTRATION Forest Plot of Indirect, 3-Node Frequentist Comparisons of De-Escalation and Short Dual Antiplatelet Therapy



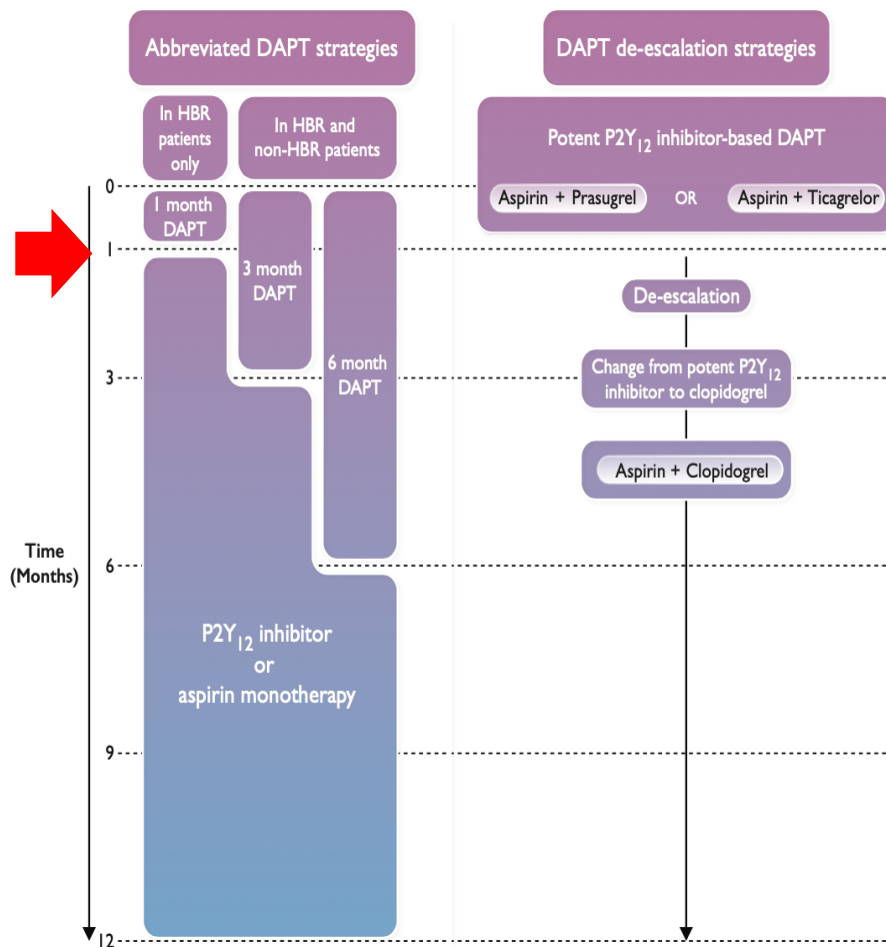
Twenty-nine studies encompassing 50,602 patients were included.



# Timing of de-escalation

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<b>Shortening/de-escalation of antithrombotic therapy</b>		
In patients who are event-free after 3–6 months of DAPT and who are not high ischaemic risk, single antiplatelet therapy (preferably with a P2Y <sub>12</sub> receptor inhibitor) should be considered. <sup>264,268–271,273,274,276,313,320</sup>	<b>IIa</b>	<b>A</b>
De-escalation of P2Y <sub>12</sub> receptor inhibitor treatment (e.g. with a switch from prasugrel/ticagrelor to clopidogrel) may be considered as an alternative DAPT strategy to reduce bleeding risk. <sup>279–282,321,322</sup>	<b>IIb</b>	<b>A</b>
In HBR patients, aspirin or P2Y <sub>12</sub> receptor inhibitor monotherapy after 1 month of DAPT may be considered. <sup>276,313</sup>	<b>IIb</b>	<b>B</b>
De-escalation of antiplatelet therapy in the first 30 days after an ACS event is not recommended. <sup>238,323</sup>	<b>III</b>	<b>B</b>

## Antiplatelet strategies to reduce bleeding risk in the first 12 months after ACS





# De-escalation o short DAPT: cosa, a chi?

- **De-escalation or short DAPT are an option to reduce bleeding risk in HBR patients.**
- **Short DAPT could represent a better approach in patients at higher risk for bleeding, such as those with high PRECISE-DAPT scores or fulfilling Academic Research Consortium high bleeding risk criteria.**
- **De-escalation resulted in larger net (ischemic/bleeding) benefit compared with SAPT.**
- **Timing: Both strategies in the first 30 days after an ACS event are NOT recommended**

# De-escalation or short DAPT?

## Personal considerations

- **De-escalation:**

**Be aware about low responders!!**

**De-Escalation PFT-guided should be considered.**

- **Short DAPT:**

**and then.... Aspirin or single PsY12 inhibitor...???**



**THANK YOU!!!!**