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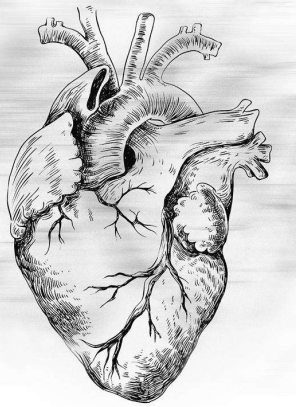

Brelor®
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ANTIPLATELET THERAPY
1ST UPDATE

Cardio_Cast

Presented by:

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THIS EPISODE'S OVERVIEW

- Antiplatelets
- Switching or De-escalation strategy
- P2Y12 inh. In ACS
- Ticagrelor Monotheapy in Complex PCI and HBR
- One month DAPT trials
- DAPT in HBR

Cardio_Cast

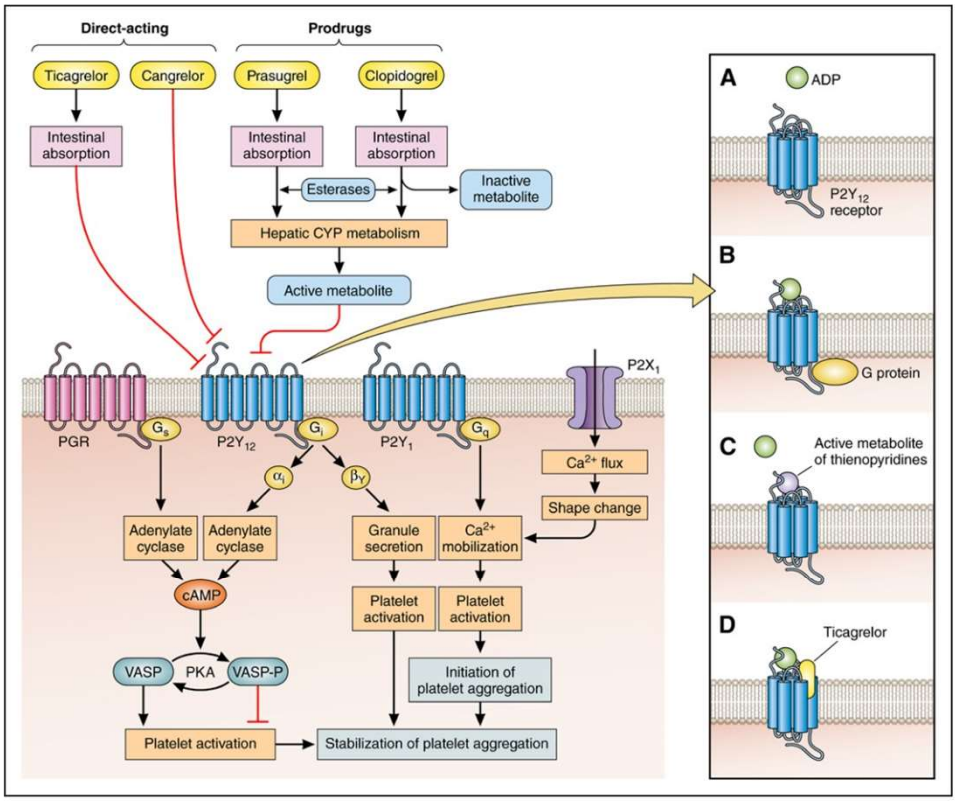


Figure 1. Mechanisms of action and binding properties of $P2Y_{12}$ inhibitors.
Left, Mechanism of action. Activation of the $P2Y_{12}$ receptor inhibits adenylyl cyclase, causing a decrease in cAMP and phosphorylated (P) vasodilator-stimulated phosphoprotein (VASP) levels, and activation of $P2Y_{12}$ causes an increase in intracellular Ca^{2+} levels. These changes promote platelet aggregation by altering the ligand-binding properties of the glycoprotein IIb/IIIa receptor. Inhibition of the $P2Y_{12}$ receptor therefore suppresses platelet activation. Clopidogrel and prasugrel are oral prodrugs requiring hepatic metabolism to generate an active metabolite that irreversibly inhibits the $P2Y_{12}$ receptor. Ticagrelor is a direct-acting (no metabolism required) oral agent that reversibly inhibits the $P2Y_{12}$ receptor. Cangrelor is a direct-acting intravenous agent that reversibly inhibits the $P2Y_{12}$ receptor. **Right**, Binding properties. **A**, ADP binds to the $P2Y_{12}$ receptor, which (**B**) leads to a conformational change of the receptor and to G-protein activation. **C**, The active metabolite of thienopyridines occupies the ADP-binding site on the $P2Y_{12}$ receptor. Binding is irreversible, which renders the receptor nonfunctional for the life of the platelet. **D**, Ticagrelor binds reversibly to the $P2Y_{12}$ receptor at a site that is distinct from the ADP-binding site. CYP indicates cytochrome P450; PGR, prostaglandin receptor; and PKA, protein kinase A. Adapted from Rollini et al[9] with permission. Copyright ©2016, Mcmillan Publishers Ltd.

Circulation. 2017;136:1955–1975. DOI: 10.1161/CIRCULATIONAHA.117.031164

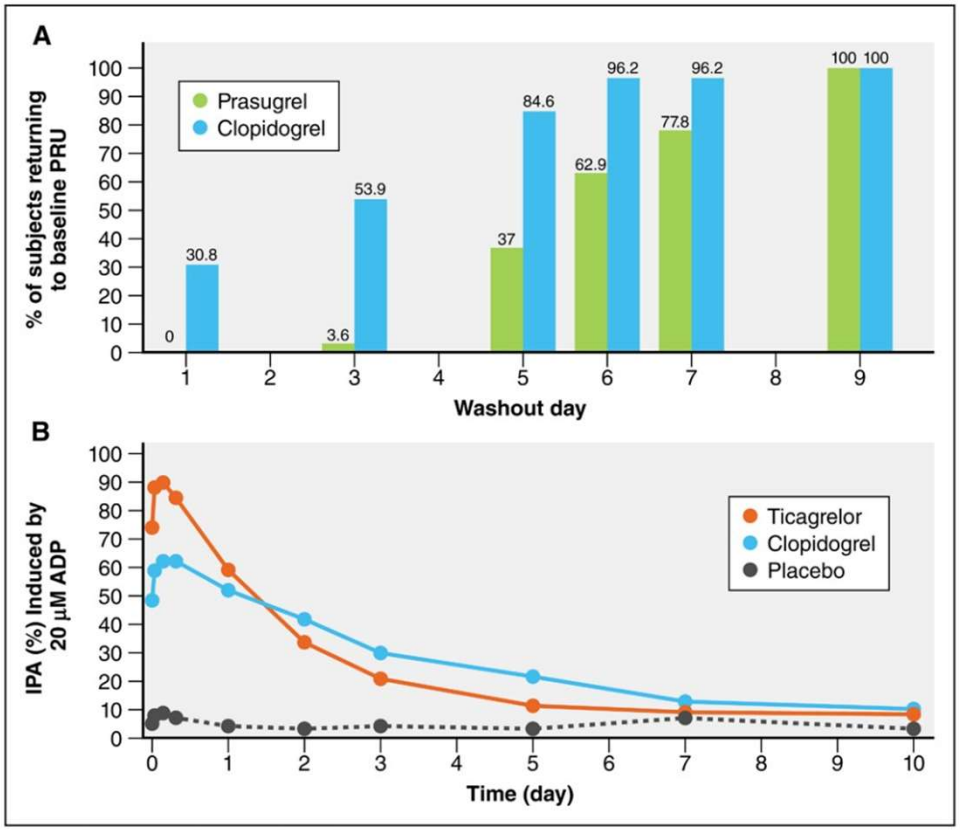


Figure 2. Offset of antiplatelet effects of oral $P2Y_{12}$ inhibitors.

A, Cumulative proportion of patients returning to baseline reactivity after thienopyridine discontinuation: the RECOVERY trial (Recovery of Platelet Function Following Discontinuation of Prasugrel or Clopidogrel Maintenance Dosing in Aspirin-Treated Subjects With Stable Coronary Disease). Baseline platelet reactivity defined as within 60 $P2Y_{12}$ reaction units (PRUs) of the reactivity measured before study drug exposure. Adapted from Price et al[14] with permission. Copyright ©2012, American College of Cardiology. **B**, Offset of inhibition of platelet aggregation (IPA) on ticagrelor, clopidogrel, and placebo: the ONSET/OFFSET study (A Study of the Onset and Offset of Antiplatelet Effects Comparing Ticagrelor, Clopidogrel, and Placebo With Aspirin). IPA after 20 µmol/L ADP (final extent) measured after last ticagrelor, clopidogrel, and placebo maintenance dose (day 0) and followed up for 10 days. Adapted from Gurbel al[16] with permission. Copyright ©2009, American Heart Association, Inc.

Circulation. 2017;136:1955–1975. DOI: 10.1161/CIRCULATIONAHA.117.031164

Table 2. Modalities of Switching Between $P2Y_{12}$ Receptor Inhibitors and Potential for DDI

Type of Pharmacodynamic Switch	Type of Drug Class Switch	Potential for DDI
Oral*		
Escalation		
Clopidogrel to prasugrel	Intraclass	No
Clopidogrel to ticagrelor	Interclass	No
De-escalation		
Prasugrel to clopidogrel	Intraclass	No
Ticagrelor to clopidogrel	Interclass	Yes
Change		
Prasugrel to ticagrelor	Interclass	No
Ticagrelor to prasugrel	Interclass	Yes
Intravenous		
Bridge		
Clopidogrel to cangrelor	Interclass	No
Prasugrel to cangrelor	Interclass	No
Ticagrelor to cangrelor	Interclass	No
Transition		
Cangrelor to clopidogrel	Interclass	Yes
Cangrelor to prasugrel	Interclass	Yes
Cangrelor to ticagrelor	Interclass	No

DDI indicates drug-drug interaction.

*Switching between oral agents may be classified according to relationship from the index event a defined as acute (<24 hours), early (1–≤30 days), late (>30 days–1 year), and very late (>1 year).

Circulation. 2017;136:1955–1975. DOI: 10.1161/CIRCULATIONAHA.117.031164

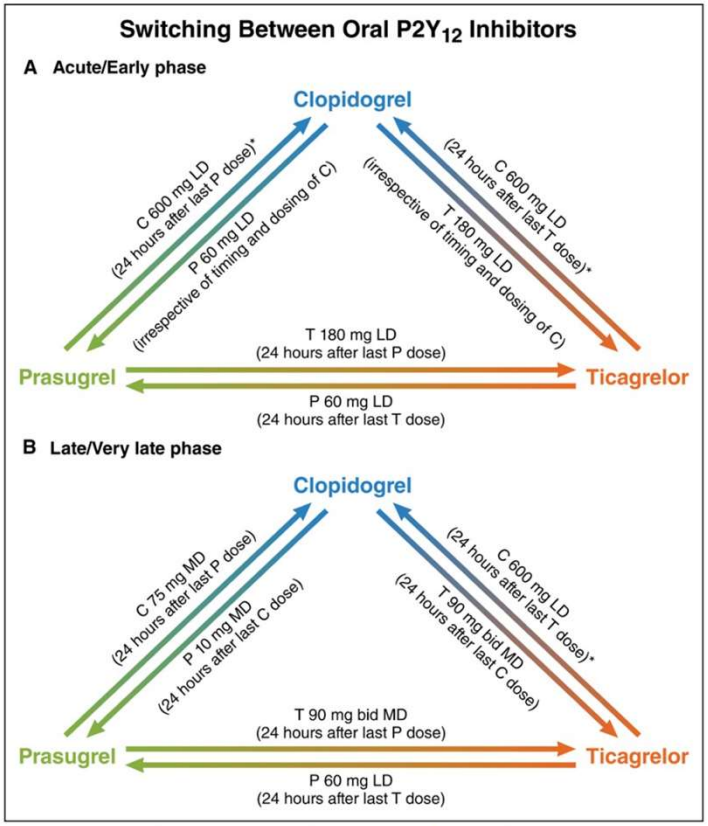


Figure 5. Consensus recommendations on switching between oral $P2Y_{12}$ inhibitors.
A, Switching between oral agents in the acute/early phase. In the acute/early phase (≤30 days from the index event), switching should occur with the administration of a loading dose (LD) in most cases, with the exception of patients who are de-escalating therapy because of bleeding or bleeding concerns, in whom a maintenance dose (MD) of clopidogrel (C) should be considered. Timing of switching should be 24 hours after the last dose of a given drug, with the exception of when escalating to prasugrel (P) or ticagrelor (T), when the LD can be given regardless of the timing and dosing of the previous clopidogrel regimen. *Consider de-escalation with clopidogrel 75-mg MD (24 hours after last prasugrel or ticagrelor dose) in patients with bleeding or bleeding concerns. **B**, Switching between oral agents in the late/very late phase. In the late/very late phase (>30 days from the index event), switching should occur with the administration of an MD 24 hours after the last dose of a given drug, with the exception of patients changing from ticagrelor to prasugrel therapy, for whom an LD should be considered. De-escalation from ticagrelor to clopidogrel should occur with administration of an LD 24 hours after the last dose of ticagrelor (but in patients in whom de-escalation occurs because of bleeding or bleeding concerns, an MD of clopidogrel should be considered). *Consider de-escalation with clopidogrel 75-mg MD (24 hours after last prasugrel or ticagrelor dose) in patients with bleeding or bleeding concerns.

Circulation. 2017;136:1955–1975. DOI: 10.1161/CIRCULATIONAHA.117.031164

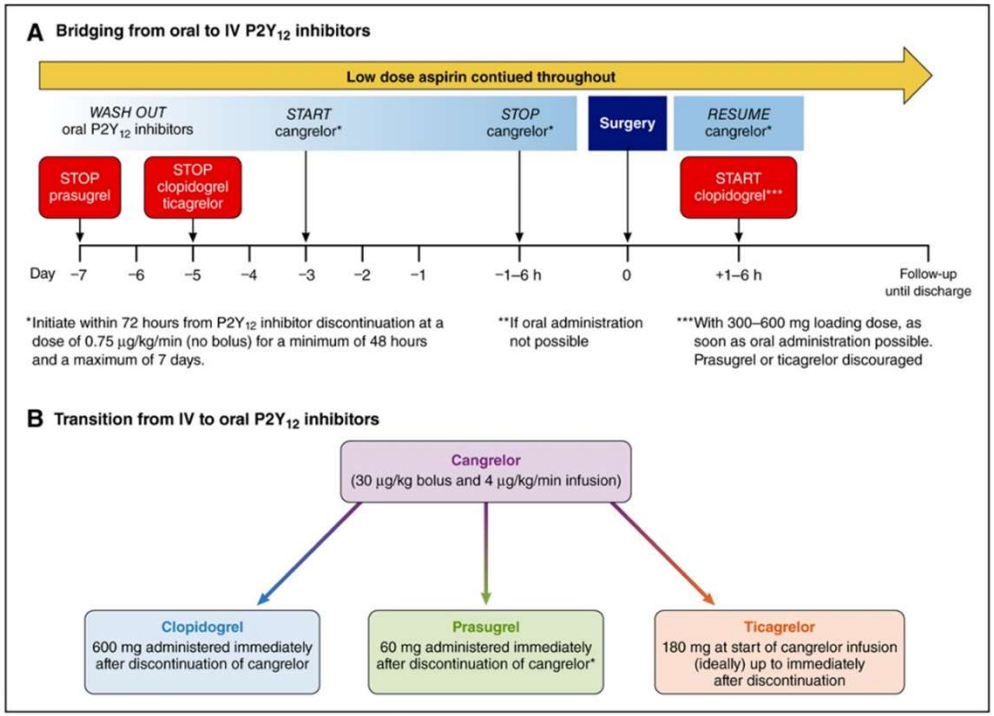


Figure 6. Consensus recommendations on switching between oral and intravenous $P2Y_{12}$ inhibitors.
A, Bridging from oral to intravenous agents. For both cardiac and noncardiac surgery, if withdrawal of $P2Y_{12}$-inhibiting therapy is needed, clopidogrel and ticagrelor should be discontinued for 5 days and prasugrel for 7 days. It is reasonable to start cangrelor bridging up to 3 to 4 days after prasugrel discontinuation and 2 to 3 days of clopidogrel and ticagrelor discontinuation. Platelet function testing may be considered to help guide timing of starting cangrelor infusion. After surgery, regardless of bridging strategy, clopidogrel should be resumed with a loading dose (LD) as soon as oral administration is possible and the risk of severe bleeding is acceptable (prasugrel and ticagrelor administration should be discouraged). If the use of oral $P2Y_{12}$-inhibiting therapy is not possible, postsurgery bridging with an intravenous agent should be considered. **B.** Transition from intravenous to oral agents. An LD should always be used when transitioning from cangrelor to an oral agent. In the case of thienopyridines (clopidogrel or prasugrel), this should be administered immediately after discontinuation of cangrelor infusion. Ticagrelor can be administered before, during, or immediately after cangrelor infusion, although earlier administration (eg, at the time of percutaneous coronary intervention) should be considered. *According to the package insert of the European Medical Agency, but not that of the US Food and Drug Administration, prasugrel may also be administered 30 minutes before infusion is stopped. Preliminary studies have shown that prasugrel given at the start of a 2-hour infusion of cangrelor results in sufficient platelet inhibition, but this strategy cannot be routinely recommended until more data are available.

Circulation. 2017;136:1955–1975. DOI: 10.1161/CIRCULATIONAHA.117.031164

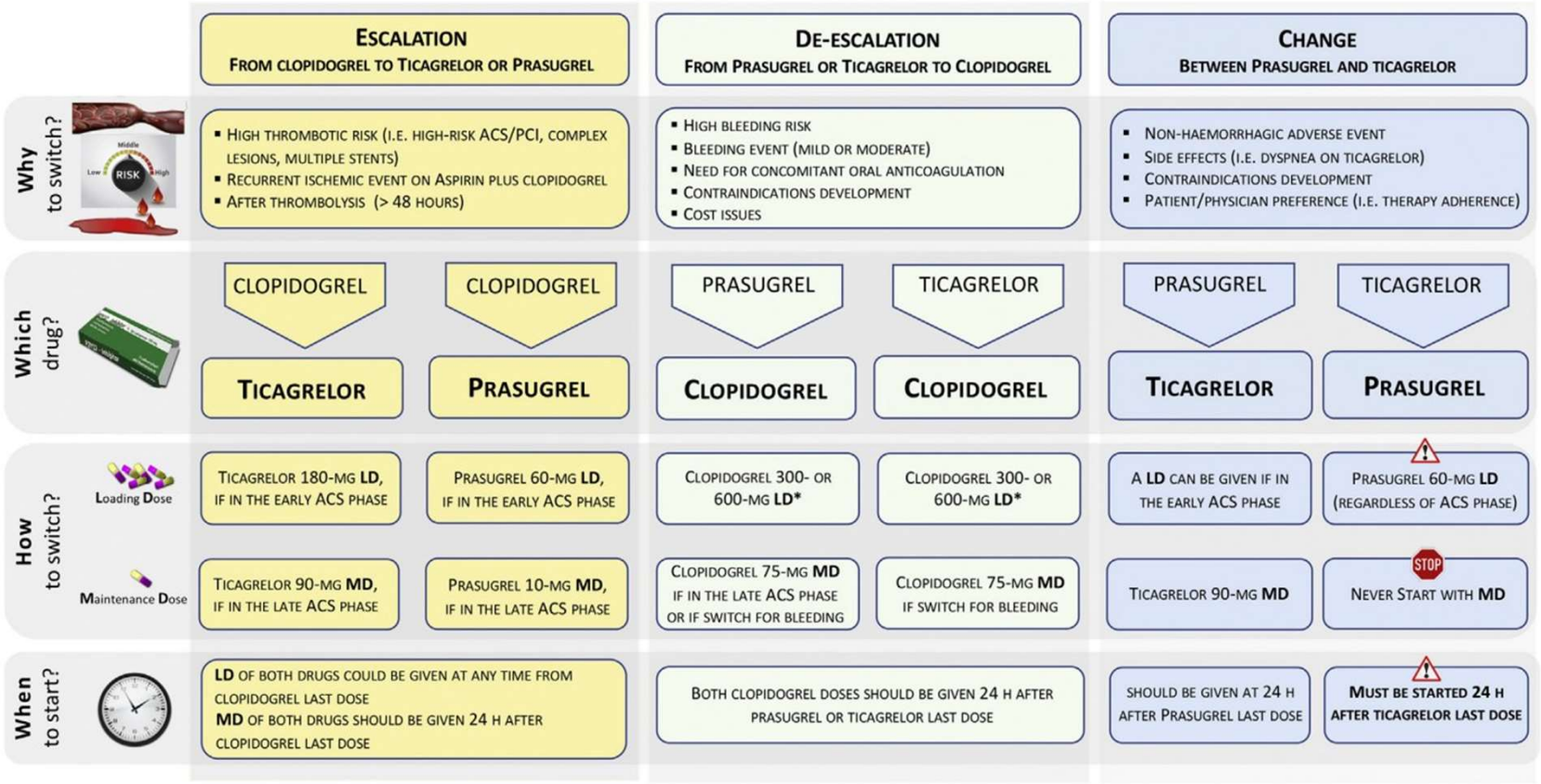


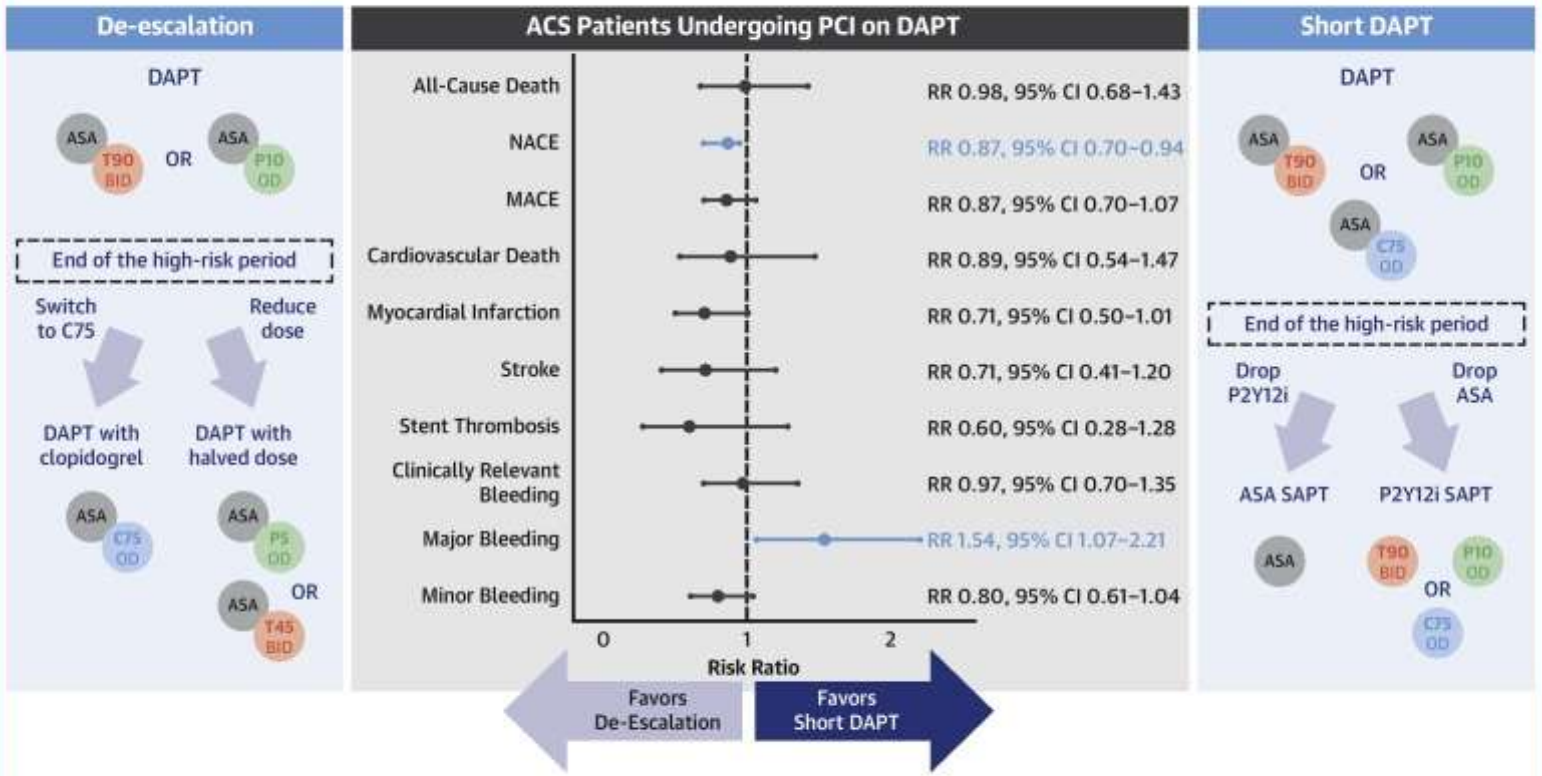
Fig. 1. Reasons and modalities for switching between oral $P2Y_{12}$ inhibitors. ACS: acute coronary syndrome; LD: loading dose; MD maintenance dose; PCI: percutaneous coronary intervention. *While a 600-mg clopidogrel loading dose should be the default strategy, a more conservative approach with a 300-mg dose could be reasonably considered if de-escalation occurs because of a particularly high bleeding risk or a bleeding event.

https://doi.org/10.1016/j.vph.2019.03.001

SHORT DURATION OF DAPT VERSUS DE-ESCALATION

- Abstract
- Objectives
- The aim of this study was to compare short dual antiplatelet therapy (DAPT) and de-escalation in a network meta-analysis using standard DAPT as common comparator.
- Background
- In patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI), shortening DAPT and de-escalating to a lower potency regimen mitigate bleeding risk. These strategies have never been randomly compared.
- Methods
- Randomized trials of DAPT modulation strategies in patients with ACS undergoing PCI were identified. All-cause death was the primary outcome. Secondary outcomes included net adverse cardiovascular events (NACE), major adverse cardiovascular events, and their components. Frequentist and Bayesian network meta-analyses were conducted. Treatments were ranked on the basis of posterior probability. Sensitivity analyses were performed to explore sources of heterogeneity.
- Results
- Twenty-nine studies encompassing 50,602 patients were included. The transitivity assumption was fulfilled. In the frequentist indirect comparison, the risk ratio (RR) for all-cause death was 0.98 (95% CI: 0.68-1.43). De-escalation reduced the risk for NACE (RR: 0.87; 95% CI: 0.70-0.94) and increased major bleeding (RR: 1.54; 95% CI: 1.07-2.21). These results were consistent in the Bayesian meta-analysis. De-escalation displayed a >95% probability to rank first for NACE, myocardial infarction, stroke, stent thrombosis, and minor bleeding, while short DAPT ranked first for major bleeding. These findings were consistent in node-split and multiple sensitivity analyses.
- Conclusions
- In patients with ACS undergoing PCI, there was no difference in all-cause death between short DAPT and de-escalation. De-escalation reduced the risk for NACE, while short DAPT decreased major bleeding. These data characterize 2 contemporary strategies to personalize DAPT on the basis of treatment objectives and risk profile.

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



Laudani, C. et al. J Am Coll Cardiol Intv. 2022;15(3):268-277.

COMPARING P2Y12 INHIBITORS IN ACUTE CORONARY SYNDROME

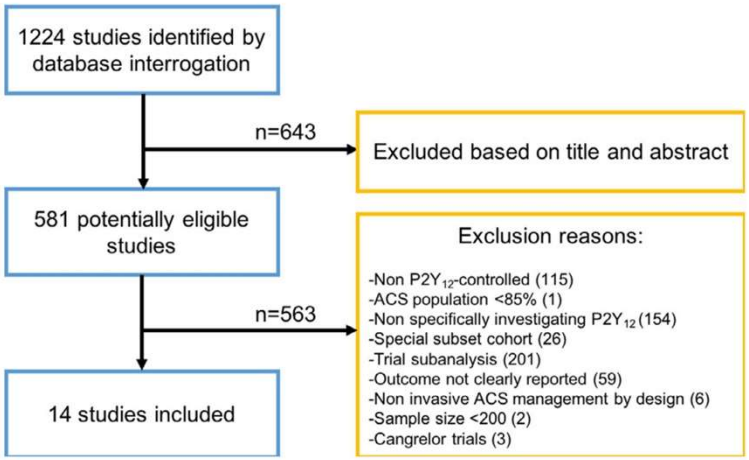


Figure 1. Consort diagram for study selection.

Summary of included studies

First Author (reference)	Year	Enrolment	Size	Design	Treatment	Population	Follow-up
Cannon[13]	2007	2004-2005	661	RCT	Ticagrelor vs Clopidogrel	STEMI, NSTEMI	30-day
Wiviott[4]	2007	2004-2007	13608	RCT	Prasugrel vs Clopidogrel	STEMI, NSTEMI, UA	Up to 15 months
Wallentin[5]	2009	2006-2008	18624	RCT	Ticagrelor vs Clopidogrel	STEMI, NSTEMI, UA	1-year
Klingenberg[14]	2015	2009-2012	2148	PR	Prasugrel vs Clopidogrel	STEMI, NSTEMI, UA	Up to 1-year
Larmore[15]	2015	2011-2013	5322	RR	Ticagrelor vs Prasugrel	STEMI, NSTEMI, UA	30-day
Goto[16]	2015	2011-2012	801	RCT	Ticagrelor vs Clopidogrel	STEMI, NSTEMI	1-year
Motovska[6]	2016	2013-2016	1230	RCT	Ticagrelor vs Prasugrel	STEMI, NSTESMI	30-day
Olier[8]	2018	2007-2014	89067	PR	Clopidogrel vs Prasugrel vs Ticagrelor	STEMI	Up to 1-year
Vos[17]	2018	2016-2013	533	PR	Ticagrelor vs Prasugrel	STEMI	1-year
Brener[18]	2019	2011-2017	1439	PR	Ticagrelor vs Clopidogrel	STEMI, NSTEMI	1-year
Schüpke[7]	2019	2013-2018	4018	RCT	Ticagrelor vs Prasugrel	STEMI, NSTEMI, UA	1-year
Krishnamurthy[9]	2019	2009-2011; 2013	4056	PR	Clopidogrel vs Prasugrel vs Ticagrelor	STEMI	Up to 1-year
De Filippo[10]	2019	2012-2016	2580	RR	Ticagrelor vs Prasugrel	STEMI, NSTEMI, UA	1-year
Welsh[11]	2019	2010-2014	9932	RCT*	Clopidogrel vs Prasugrel vs Ticagrelor	STEMI	1-year

NSTEMI = non ST-elevation myocardial infarction; PR = prospective registry; RCT = randomized clinical trial; RR = retrospective registry; STEMI = ST-elevation myocardial infarction; UA = unstable angina.

* randomization according to routine upfront manual thrombectomy versus PCI alone.

https://doi.org/10.1016/j.amjcard.2020.03.019

Cardio_Cast

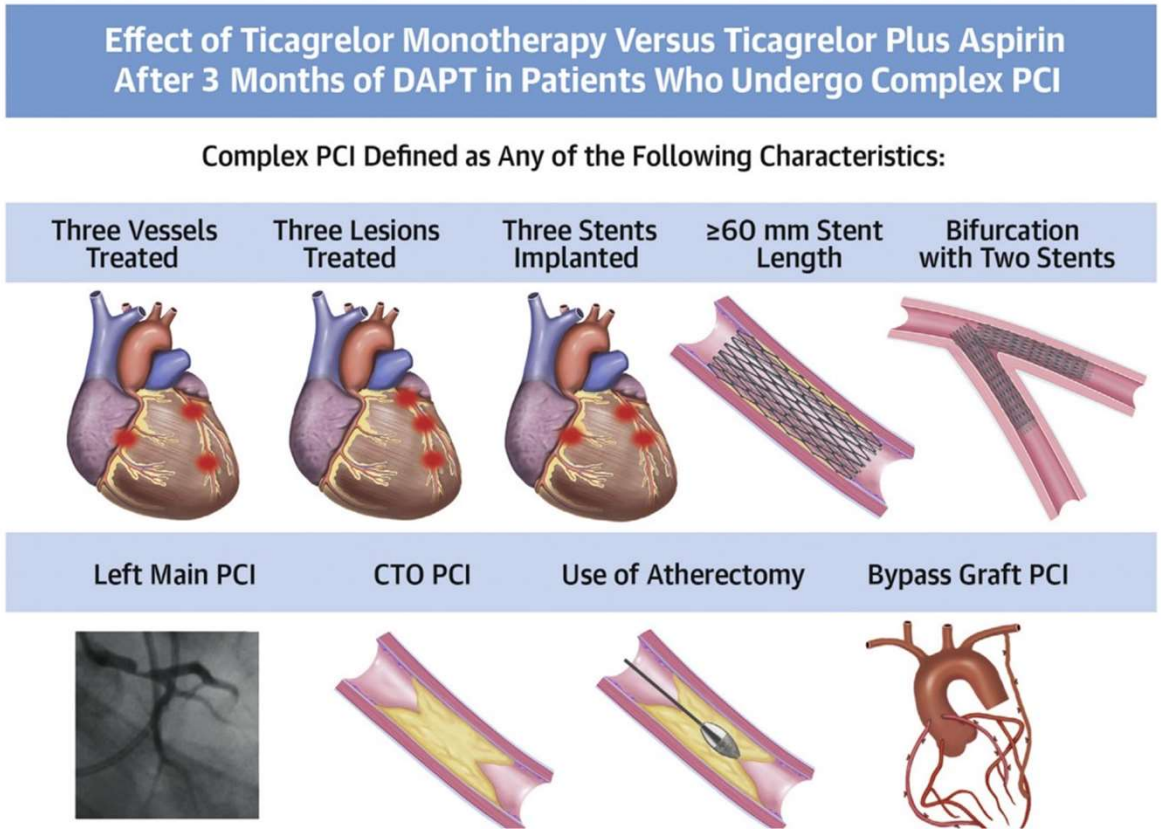
League table with respect of 1-year outcomes

Clopidogrel	Ticagrelor	Prasugrel
1-year major adverse cardiovascular events		
Clopidogrel	0.82 (0.60,1.10)	0.81 (0.60,1.11)
1.22 (0.91,1.65)	Ticagrelor	1.00 (0.73,1.36)
1.23 (0.90,1.68)	1.00 (0.74,1.37)	Prasugrel
1-year all-cause death		
Clopidogrel	0.77 (0.62,0.95)	0.62 (0.50,0.78)
1.30 (1.05,1.61)	Ticagrelor	0.81 (0.65,1.01)
1.61 (1.29,2.01)	1.24 (0.99,1.55)	Prasugrel
1-year myocardial infarction		
Clopidogrel	0.81 (0.61,1.08)	0.69 (0.52,0.92)
1.23 (0.93,1.64)	Ticagrelor	0.85 (0.64,1.14)
1.45 (1.09,1.92)	1.17 (0.88,1.57)	Prasugrel
1-year major bleeding		
Clopidogrel	1.08 (0.76,1.54)	0.97 (0.68,1.40)
0.92 (0.65,1.31)	Ticagrelor	0.90 (0.62,1.29)
1.03 (0.72,1.48)	1.11 (0.77,1.60)	Prasugrel

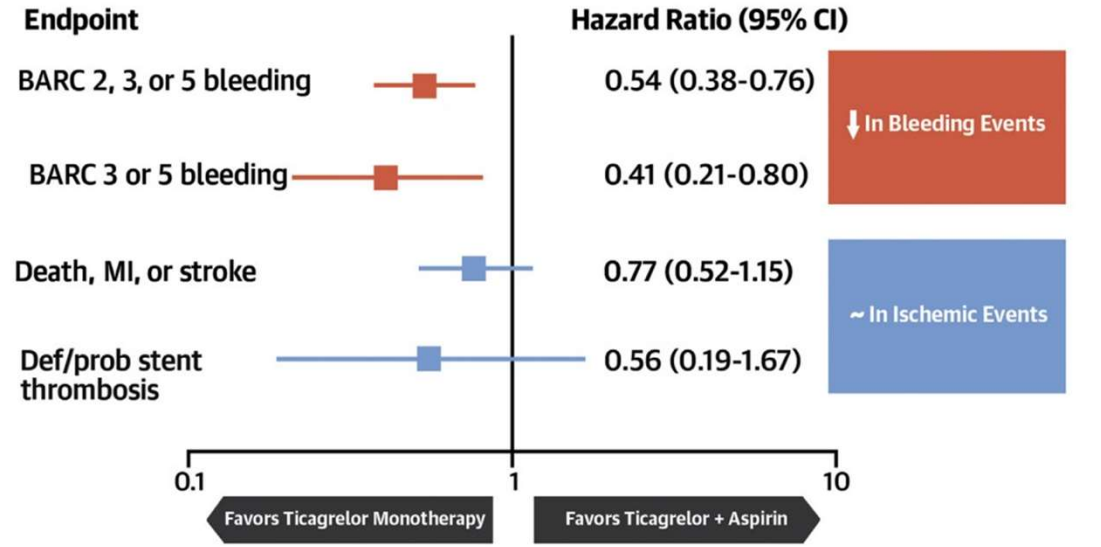
Values are expressed as OR.

https://doi.org/10.1016/j.amjcard.2020.03.019

CENTRAL ILLUSTRATION Ticagrelor With or Without Aspirin After Complex Percutaneous Coronary Intervention



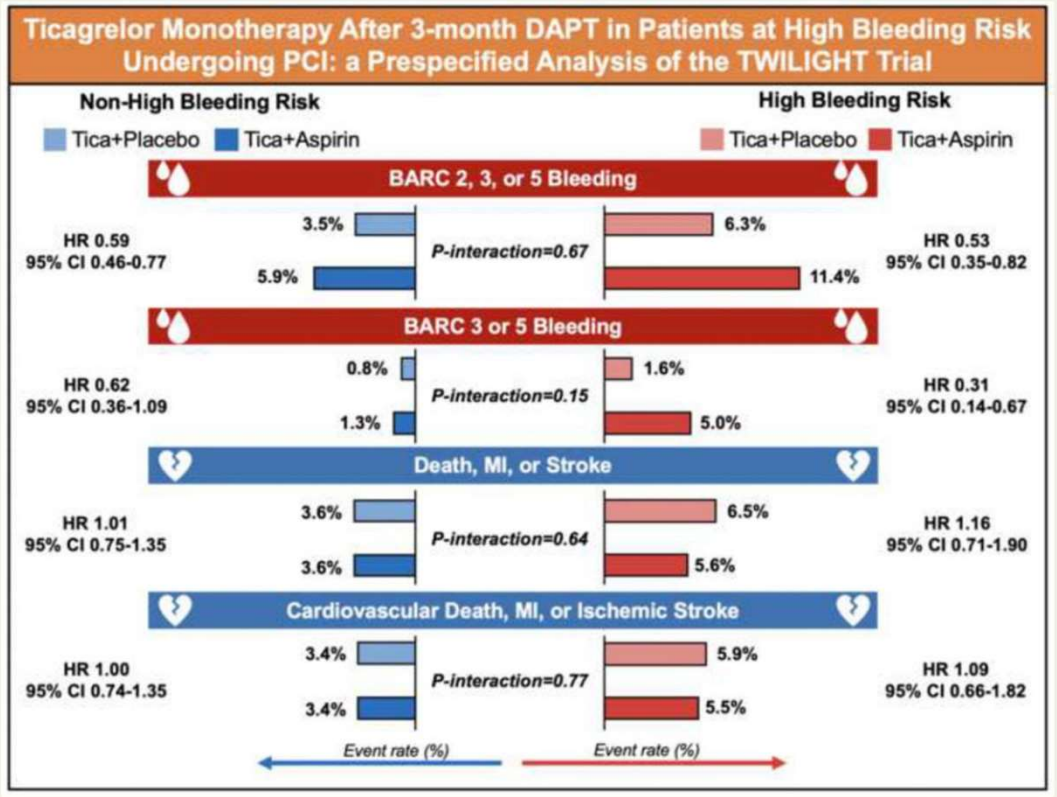
Risk of Adverse Events 12 Months After Randomization in Patients Undergoing Complex PCI



Dangas, G. et al. J Am Coll Cardiol. 2020;75(19):2414-24.

Complex PCI was defined as any of the following: 3 vessels treated, ≥3 lesions treated, total stent length >60 mm, bifurcation with 2 stents implanted, atherectomy device use, left main PCI, surgical bypass graft or chronic total occlusion as target lesions. Following 3 months of adherence to DAPT post-PCI and in the absence of major bleeding or ischemic events, this post hoc analysis from the TWILIGHT trial assessing clinical outcomes in patients who underwent complex PCI (n = 2,342) showed that ticagrelor monotherapy, compared with ticagrelor plus aspirin, was associated with a 46% reduction in the incidence of BARC 2, 3, or 5 bleeding over 1 year. There was no significant difference in the 1-year rate of all-cause death, MI, or stroke between the 2 treatment arms. CI = confidence interval; CTO =chronic total occlusion; DAPT = dual antiplatelet therapy; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Graphical Abstract



Effects of ticagrelor plus placebo vs. ticagrelor plus aspirin on bleeding and ischaemic events among high bleeding risk and non-high bleeding risk patients who tolerated 3 months of dual antiplatelet therapy after percutaneous coronary intervention with a drug-eluting stent. BARC, Bleeding Academic Research Consortium; CI, confidence interval; DAPT, dual antiplatelet therapy; HBR, high bleeding risk; HR, hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention; tica, ticagrelor.

https://doi.org/10.1093/eurheartj/ehab658

Bleeding events	No. of patients	Tica+Placebo no. of events (%)	Tica+Aspirin no. of events (%)	HR (95% CI)	Interaction p-value
BARC 2, 3, or 5					
Non-HBR	5114	89 (3.5%)	148 (5.9%)	0.59 (0.46 - 0.77)	0.673
HBR	1064	32 (6.3%)	61 (11.4%)	0.53 (0.35 - 0.82)	
BARC 3, or 5					
Non-HBR	5114	20 (0.8%)	32 (1.3%)	0.62 (0.36 - 1.09)	0.148
HBR	1064	8 (1.6%)	27 (5.0%)	0.31 (0.14 - 0.67)	
TIMI major					
Non-HBR	5114	13 (0.5%)	17 (0.7%)	0.76 (0.37 - 1.57)	0.080
HBR	1064	2 (0.4%)	12 (2.2%)	0.17 (0.04 - 0.78)	
GUSTO moderate or severe					
Non-HBR	5114	14 (0.6%)	17 (0.7%)	0.82 (0.41 - 1.67)	0.109
HBR	1064	8 (1.6%)	24 (4.5%)	0.35 (0.16 - 0.77)	
ISTH major					
Non-HBR	5114	22 (0.9%)	35 (1.4%)	0.63 (0.37 - 1.07)	0.203
HBR	1064	9 (1.8%)	27 (5.0%)	0.35 (0.16 - 0.73)	

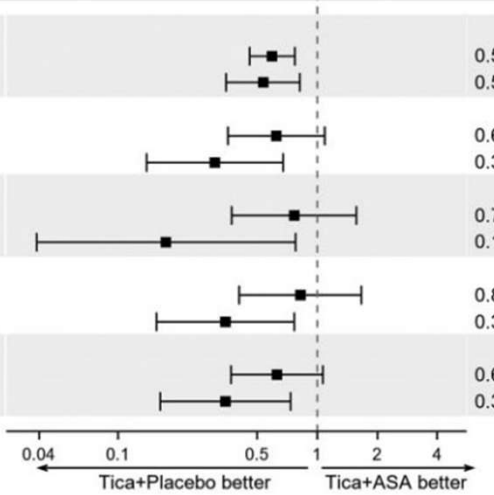


Figure 2 Risk of bleeding events at 1 year. Forest plot showing the effect of ticagrelor plus placebo vs. ticagrelor plus aspirin on the bleeding endpoints according to high bleeding risk status. Bleeding outcomes were analysed in the intention-to-treat cohort. BARC, Bleeding Academic Research Consortium; CI, confidence interval; GUSTO, Global Use of Strategies to Open Occluded Arteries; HBR, high bleeding risk; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis; TIMI, Thrombolysis in Myocardial Infarction.

https://doi.org/10.1093/eurheartj/ehab658

Ischemic events	No. of patients	Tica+Placebo no. of events (%)	Tica+Aspirin no. of events (%)	HR (95% CI)	Interaction p-value
Death. MI or stroke					
Non-HBR	5066	91 (3.6%)	90 (3.6%)	1.01 (0.75 - 1.35)	0.637
HBR	1051	33 (6.5%)	30 (5.6%)	1.16 (0.71 - 1.90)	
CV-death, MI or ischemic stroke					
Non-HBR	5066	85 (3.4%)	85 (3.4%)	1.00 (0.74 - 1.35)	0.771
HBR	1051	30 (5.9%)	29 (5.5%)	1.09 (0.66 - 1.82)	
All-cause death					
Non-HBR	5066	21 (0.8%)	26 (1.0%)	0.81 (0.45 - 1.43)	0.942
HBR	1051	12 (2.3%)	16 (3.0%)	0.78 (0.37 - 1.64)	
CV-death					
Non-HBR	5066	16 (0.6%)	21 (0.8%)	0.76 (0.40 - 1.46)	0.820
HBR	1051	9 (1.8%)	14 (2.6%)	0.67 (0.29 - 1.55)	
MI					
Non-HBR	5066	65 (2.6%)	63 (2.5%)	1.03 (0.73 - 1.46)	0.551
HBR	1051	23 (4.5%)	19 (3.6%)	1.27 (0.69 - 2.34)	
Ischemic stroke					
Non-HBR	5066	10 (0.4%)	5 (0.2%)	2.00 (0.68 - 5.84)	0.972
HBR	1051	2 (0.4%)	1 (0.2%)	2.10 (0.19 - 23.1)	
Definite/probable ST					
Non-HBR	5066	10 (0.4%)	15 (0.6%)	0.66 (0.30 - 1.48)	0.393
HBR	1051	4 (0.8%)	3 (0.6%)	1.40 (0.31 - 6.24)	

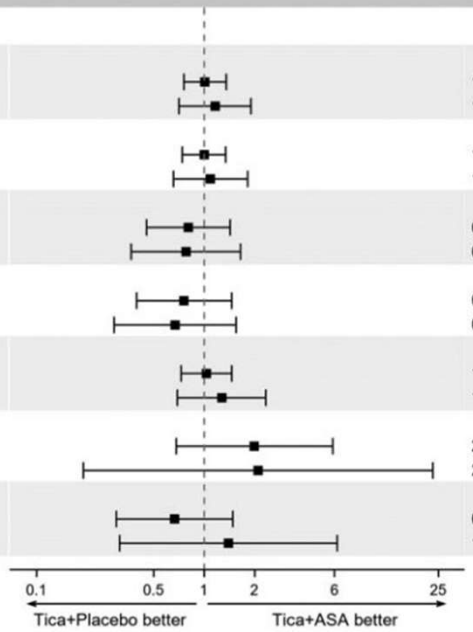


Figure 4 Risk of ischaemic events at 1 year. Forest plot showing the effect of ticagrelor plus placebo vs. ticagrelor plus aspirin on the ischaemic endpoints according to high bleeding risk status. Ischaemic outcomes were analysed in the per-protocol cohort. CI, confidence interval, CV, cardiovascular, HBR, high bleeding risk; HR, hazard ratio, MI, myocardial infarction, ST, stent thrombosis.

https://doi.org/10.1093/eurheartj/ehab658

ONE-MONTH DUAL ANTIPLATELET THERAPY ONYX ONE

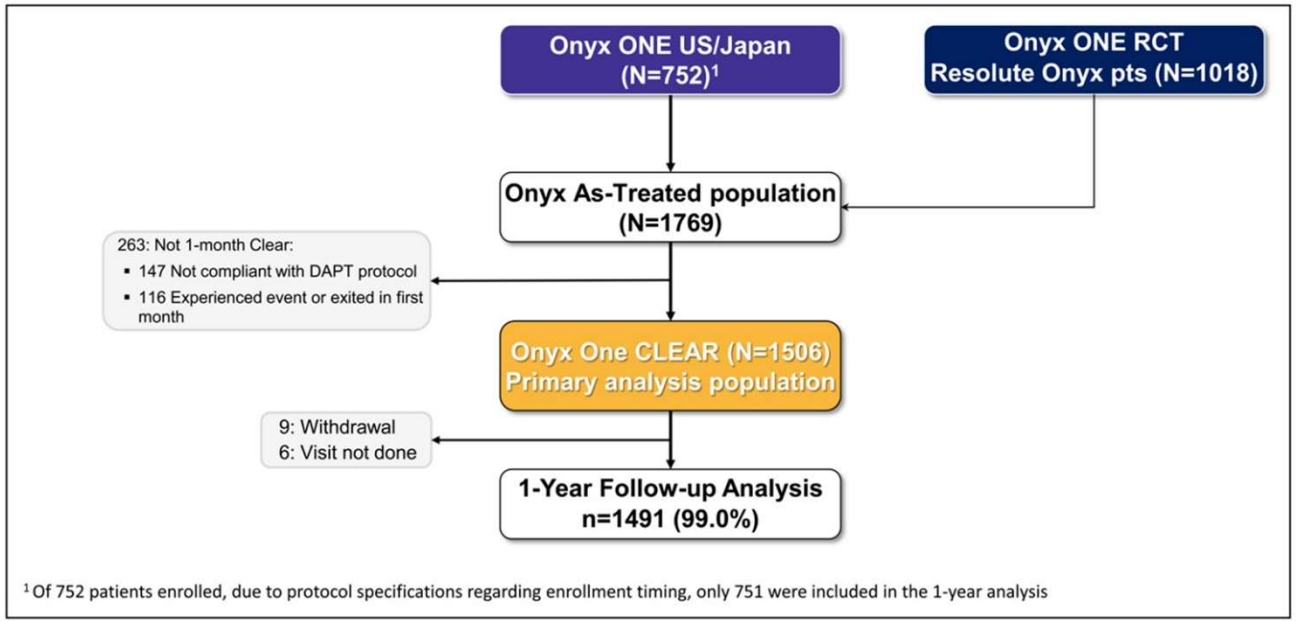
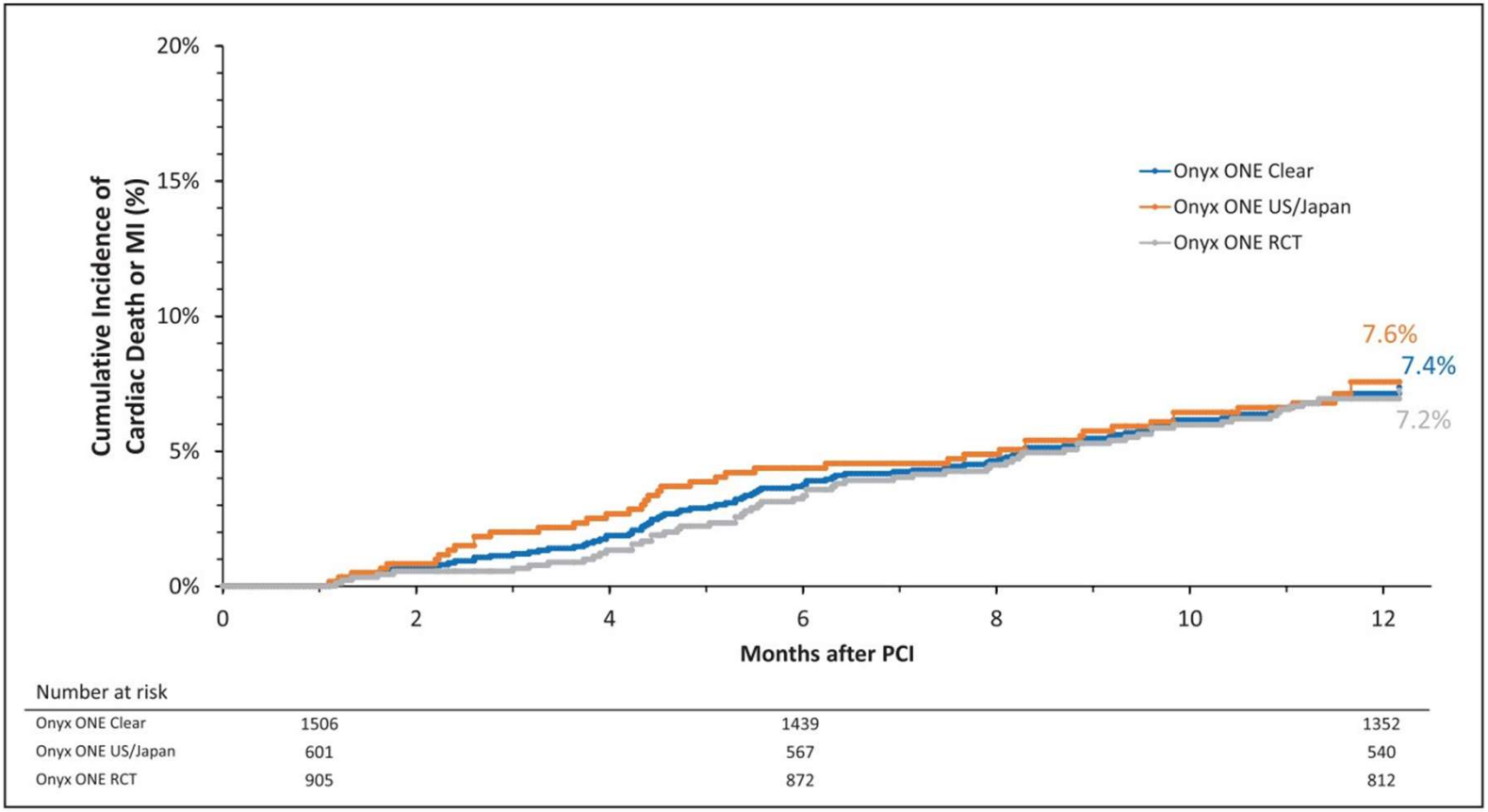


Figure 1. Patient flowchart.
DAPT indicates dual antiplatelet therapy; pts, patients; and RCT, randomized clinical trial.

10.1161/CIRCINTERVENTIONS.120.009565

- BACKGROUND: Despite treatment guidance endorsing shortened dual antiplatelet therapy (DAPT) duration in high bleeding risk (HBR) patients after drug-eluting stents, limited evidence exists to support these recommendations. The present study was designed to examine the safety and effectiveness of 1-month DAPT duration following percutaneous coronary intervention with zotarolimus-eluting stents in HBR patients.
- METHODS: Onyx ONE Clear was a prospective, multicenter, nonrandomized study evaluating the safety and effectiveness of 1-month DAPT followed by single antiplatelet therapy in HBR patients undergoing percutaneous coronary intervention with Resolute Onyx drug-eluting stents. The primary analysis of cardiac death or myocardial infarction between 1 month and 1 year was performed in the prespecified one-month clear population of patients pooled from the Onyx ONE US/Japan study and Onyx ONE randomized controlled trial. One-month clear was defined as DAPT adherence and without major adverse events during the first month following percutaneous coronary intervention.
- RESULTS: Among patients enrolled in Onyx ONE US/Japan (n=752) and Onyx ONE randomized controlled trial (n=1018), 1506 patients fulfilled one-month clear criteria. Mean HBR characteristics per patient was 1.6 with 44.7% having multiple risks. By 2 months and 1 year, respectively, 96.9% and 89.3% of patients were taking single antiplatelet therapy. Between 1 month and 1 year, the rate of the primary end point was 7.0%. The 1-sided upper 97.5% CI was 8.4%, less than the performance goal of 9.7% (P less than 0.001)
- CONCLUSIONS: Among HBR patients who were event free before DAPT discontinuation at 1 month, favorable safety and effectiveness through 1 year support treatment with Resolute Onyx drug-eluting stents as part of an individualized strategy for shortened DAPT duration following percutaneous coronary intervention.

10.1161/CIRCINTERVENTIONS.120.009565



Number at risk			
Onyx ONE Clear	1506	1439	1352
Onyx ONE US/Japan	601	567	540
Onyx ONE RCT	905	872	812

Figure 3. Kaplan-Meier rates of cardiac death or myocardial infarction (MI) for patients in Onyx ONE Clear, Onyx ONE US/Japan, and Onyx ONE randomized controlled trial (RCT) study populations.
The Onyx ONE Clear population is comprised of the one-month clear populations from Onyx ONE RCT and Onyx ONE US/Japan. PCI indicates percutaneous coronary intervention.

10.1161/CIRCINTERVENTIONS.120.009565

ONE-MONTH DAPT TRIAL

ABSTRACT

OBJECTIVES The aim of this study was to determine whether 1 month of dual-antiplatelet therapy (DAPT) followed by aspirin monotherapy after polymer-free drug-coated stent (PF-DCS) implantation is noninferior to 6 to 12 months of DAPT after biodegradable-polymer drug-eluting stent (BP-DES) implantation.

BACKGROUND It is necessary to determine the optimal minimal duration of DAPT followed by aspirin monotherapy after percutaneous coronary intervention (PCI).

METHODS In this trial, 3,020 patients with coronary artery disease considered for PCI for noncomplex lesions were randomized to 1-month DAPT after PF-DCS (n = 1,507) or 6- to 12-month DAPT after BP-DES (n = 1,513). The primary endpoint was the 1-year composite of cardiac death, nonfatal myocardial infarction, target vessel revascularization, stroke, or major bleeding (noninferiority hypothesis margin of 3%).

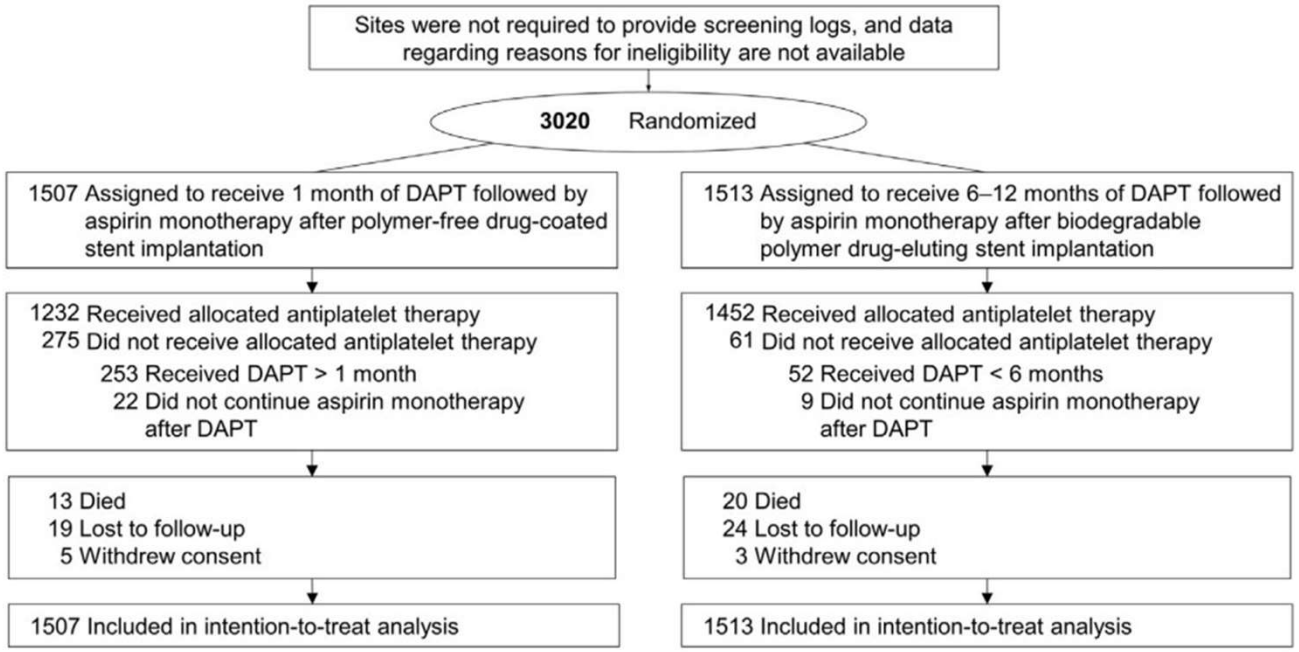
RESULTS The primary endpoint occurred in 88 patients (5.9%) in the 1-month DAPT after PF-DCS group and 98 patients (6.5%) in the 6- to 12-month DAPT after BP-DES group (absolute difference −0.7%; upper limit of 1-sided 97.5% confidence interval: 1.33%; $P < 0.001$ for noninferiority). The occurrence of major bleeding was not different (1.7% vs 2.5%; $P = 0.136$). There was no difference in the occurrence of stent thrombosis (0.7% vs 0.8%; $P = 0.842$).

CONCLUSIONS Among patients who underwent PCI for noncomplex lesions, 1-month DAPT followed by aspirin monotherapy after PF-DCS implantation was noninferior to 6- to 12-month DAPT after BP-DES implantation for the 1-year composite of cardiovascular events or major bleeding. The present findings need to be interpreted in the setting of different types of stents according to antiplatelet strategy. (A Randomized Controlled Comparison Between One Versus More Than Six Months of Dual Antiplatelet Therapy After Biolimus A9-Eluting Stent Implantation; NCT02513810)

(J Am Coll Cardiol Intv 2021;14:1801–1811)

https://doi.org/10.1016/j.jcin.2021.06.003

FIGURE 1 **Trial Profile**



DAPT = dual-antiplatelet therapy.

https://doi.org/10.1016/j.jcin.2021.06.003

TABLE 3 Clinical Outcomes at 1 Year

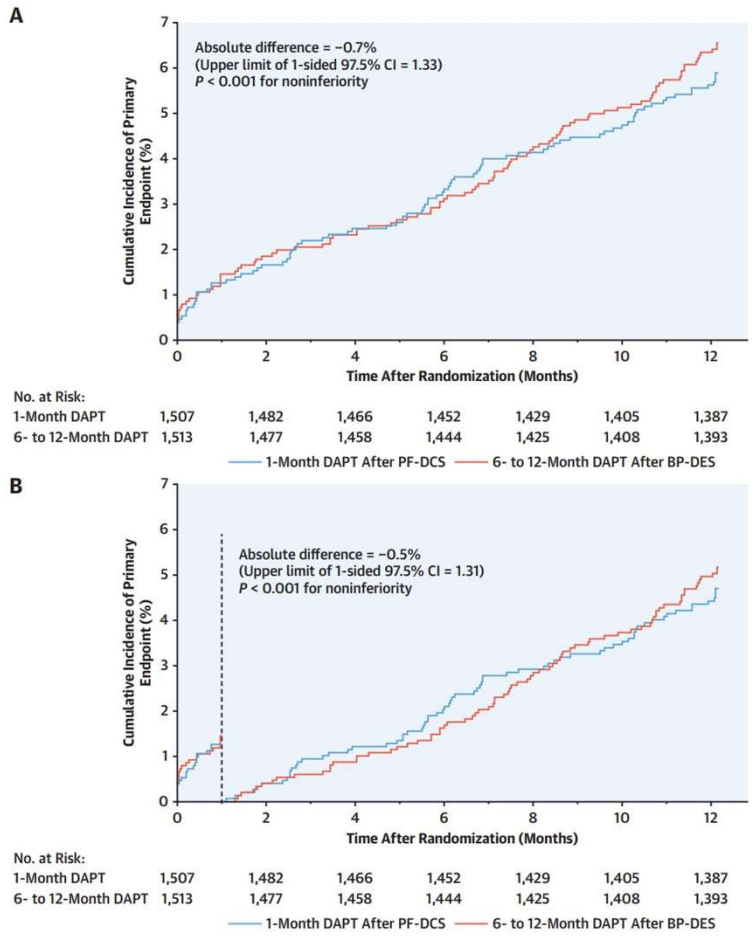
	1-Month DAPT After PF-DCS (n = 1,507)	6- to 12-Month DAPT After BP-DES (n = 1,513)	Absolute Difference (Confidence Interval*)	*P* Value†	Hazard Ratio (95% Confidence Interval)	*P* Value‡
Primary endpoint						
Composite of cardiac death, nonfatal myocardial infarction, target vessel revascularization, stroke, or major bleeding	88 (5.9)	98 (6.5)	−0.7 (1.3)	<0.001	0.90 (0.68 to 1.20)	0.475
Secondary endpoints						
All-cause death	13 (0.9)	20 (1.3)	−0.5 (−1.2 to 0.3)	—	0.65 (0.32 to 1.31)	0.225
Cardiac death	6 (0.4)	10 (0.7)	−0.3 (−0.8 to 0.3)	—	0.60 (0.22 to 1.66)	0.321
Nonfatal myocardial infarction	17 (1.1)	22 (1.5)	−0.3 (−1.1 to 0.5)	—	0.78 (0.41 to 1.46)	0.426
Target vessel revascularization	41 (2.8)	39 (2.6)	0.1 (−1.0 to 1.3)	—	1.05 (0.68 to 1.63)	0.814
Stent thrombosis	11 (0.7)	12 (0.8)	−0.1 (−0.7 to 0.6)	—	0.90 (0.41 to 2.09)	0.842
Definite	7	6				
Probable	4	6				
Stroke	13 (0.9)	16 (1.1)	−0.2 (−0.9 to 0.5)	—	0.81 (0.39 to 1.69)	0.581
Ischemic	9	5				
Hemorrhagic	4	11				
Major bleeding	26 (1.7)	38 (2.5)	−0.8 (−1.8 to 0.2)	—	0.69 (0.42 to 1.13)	0.136

Values are n (cumulative incidence, %). The cumulative incidences are calculated by Kaplan-Meier estimates. *Upper limit of 1-sided 97.5% confidence interval data for the primary endpoint; 95% confidence interval for other outcomes. †For noninferiority. ‡For superiority.

Abbreviations as in Table 1.

https://doi.org/10.1016/j.jcin.2021.06.003

CENTRAL ILLUSTRATION Kaplan-Meier Curves of the Primary Endpoint



Hong, S.-J. et al. J Am Coll Cardiol Intv. 2021;14(16):1801-1811.

(A) Cumulative incidence of primary endpoint (composite of cardiac death, nonfatal myocardial infarction, target vessel revascularization, stroke, or major bleeding). **(B)** One-month landmark analysis for the primary endpoint. BP-DES = biodegradablepolymer drug-eluting stent(s); DAPT = dual-antiplatelet therapy; PF-DCS = polymer-free drugcoated stent(s).

https://doi.org/10.1016/j.jcin.2021.06.003

DUAL ANTIPLATELET THERAPY AFTER PCI IN PATIENTS AT HIGH BLEEDING RISK

Cardio_Cast

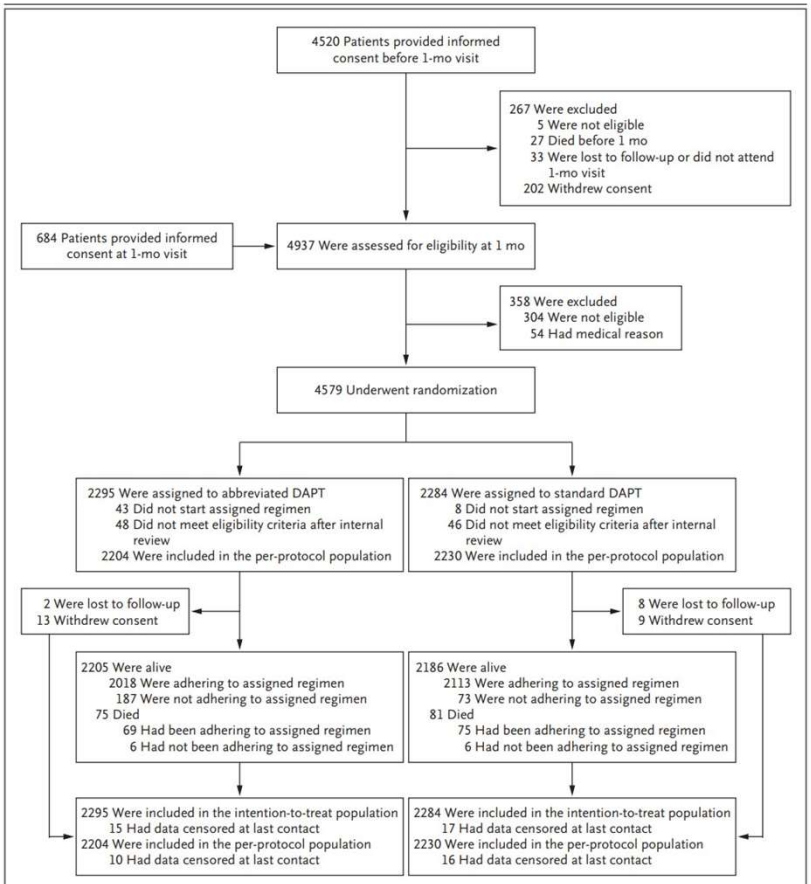
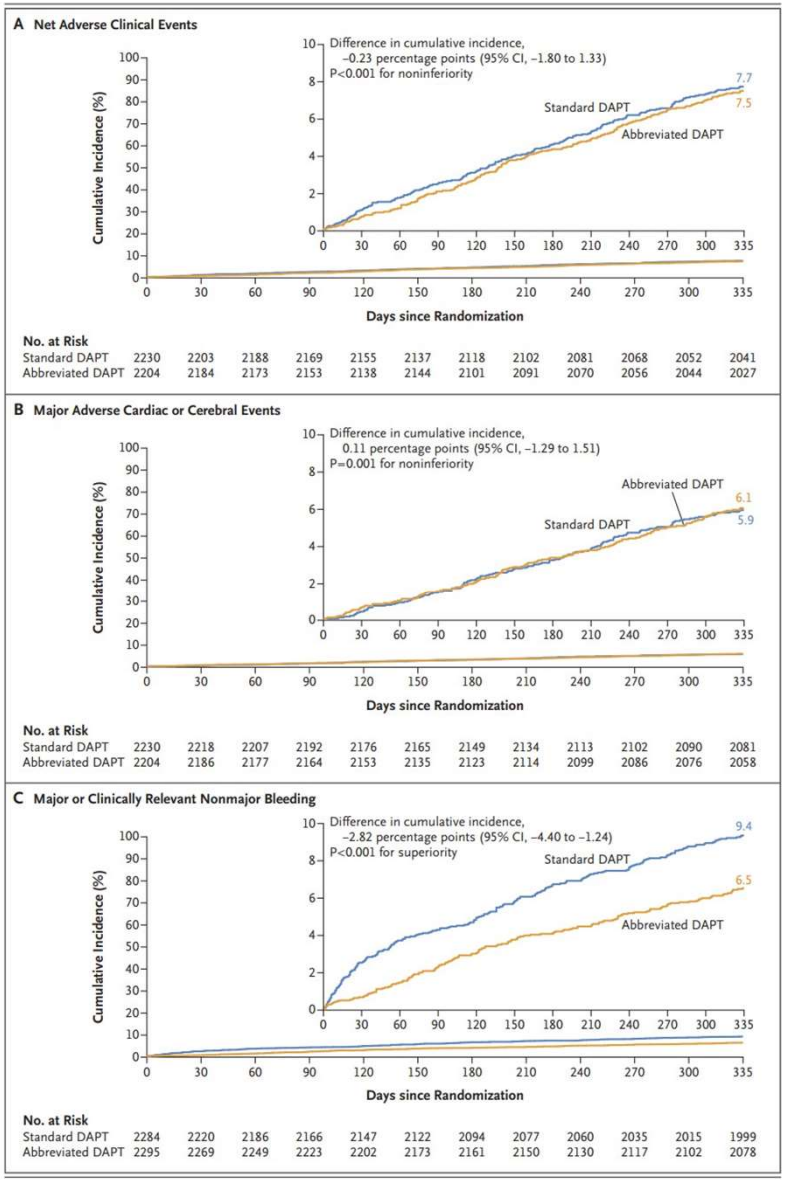


Figure 1. Randomization, Treatment, and Follow-up of the Patients.

Patients provided written informed consent either during the interval between the index percutaneous coronary intervention and the 1-month randomization visit or at the 1-month visit. Patients who provided consent before the 1-month visit could later be excluded (e.g., for death or withdrawal of consent), whereas those who provided consent at the 1-month visit were all included in the trial. Patients who did not start the assigned antiplatelet regimen were those who did not start the regimen within 14 days after randomization or who started a nonallowed regimen owing to an event occurring within 14 days after randomization. Patients who are indicated as receiving the assigned antiplatelet regimen were those who were noted as adhering to the regimen on day 335; if the information was not recorded on day 335, the latest available information on adherence was used. In the per-protocol population, one patient in the abbreviated-therapy group was lost to follow-up and nine withdrew consent; in the standard-therapy group, seven patients were lost to follow-up and nine withdrew consent. DAPT denotes dual antiplatelet therapy.

10.1056/NEJMoa2108749

Cumulative Incidence of Three Primary Composite Outcomes at 335 Days. The three ranked primary outcomes were a composite of death from any cause, myocardial infarction, stroke, or major bleeding (net adverse clinical events), which was assessed in the per-protocol population (Panel A); a composite of death from any cause, myocardial infarction, or stroke (major adverse cardiac or cerebral events), which was assessed in the per-protocol population (Panel B); and major or clinically relevant nonmajor bleeding, which was assessed in the intention-to-treat population (Panel C). The per-protocol population excluded patients who did not fulfill the selection criteria or did not implement protocol-mandated therapy within 14 days after randomization. The intention-to-treat population included all the patients who underwent randomization. Insets show the same data on enlarged y axes



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