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STATE OF THE ART REVIEW
Thrombosis and antithrombotic treatment

Aspirin-free antiplatelet strategies after percutaneous coronary interventions

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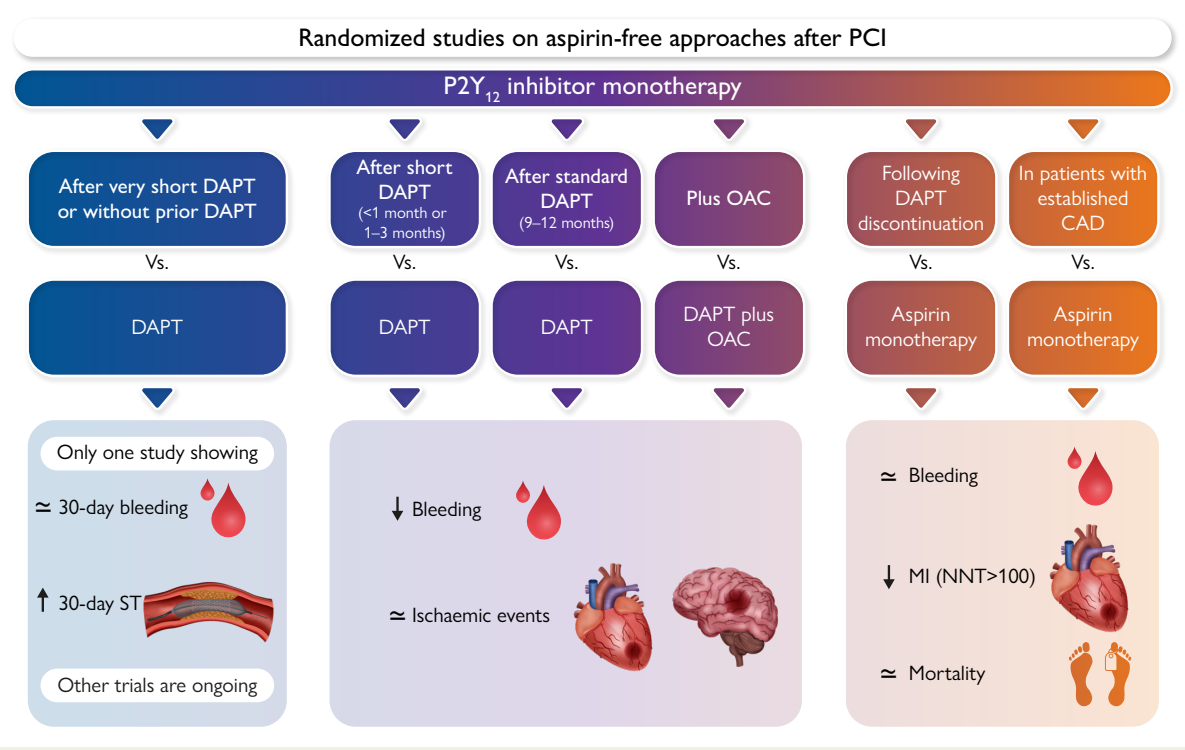
Graphical Abstract



Studies on aspirin-free antiplatelet approaches after percutaneous coronary intervention (PCI) can be divided into two groups: (i) those comparing $P2Y_{12}$ inhibitor monotherapy vs. dual antiplatelet therapy (DAPT) after PCI in patients with and without concomitant indication for oral anticoagulation (OAC) and (ii) those comparing $P2Y_{12}$ inhibitor monotherapy vs. aspirin monotherapy after DAPT discontinuation or in patients with established coronary artery disease (CAD), including prior PCI patients. Among studies of the first group, one recent study assessing an aspirin-free treatment since the PCI time has shown that monotherapy with low-dose prasugrel vs. DAPT was associated with increased 30-day thrombotic events; other studies assessing the $P2Y_{12}$ inhibitor monotherapy after very short DAPT limited to the peri-PCI time are ongoing. The other studies of the first group have shown that $P2Y_{12}$ inhibitor monotherapy following a short course of DAPT after PCI (<1 month in one study and 1–3 months in most studies) or combined with OAC was associated with decreased bleeding and similar overall ischaemic events compared with conventional DAPT. Overall studies of the second group have shown that $P2Y_{12}$ inhibitor monotherapy (clopidogrel or ticagrelor) vs. aspirin was associated with similar bleeding, reduced myocardial infarction (MI) with a number needed to treat (NNT) > 100 across studies, and comparable mortality. ST, stent thrombosis.

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Abstract

Dual antiplatelet therapy (DAPT) with aspirin and a platelet $P2Y_{12}$ receptor inhibitor is the standard antithrombotic treatment after percutaneous coronary interventions (PCI). Several trials have challenged guideline-recommended DAPT after PCI by testing the relative clinical effect of an aspirin-free antiplatelet approach—consisting of $P2Y_{12}$ inhibitor monotherapy after a short course (mostly 1–3 months) of DAPT—among patients undergoing PCI without a concomitant indication for oral anticoagulation (OAC). Overall, these studies have shown $P2Y_{12}$ inhibitor monotherapy after short DAPT to be associated with a significant reduction in the risk of bleeding without an increase in thrombotic or ischaemic events compared with continued DAPT. Moreover, the effects of the $P2Y_{12}$ inhibitor monotherapy without prior DAPT or following a very short course of DAPT after PCI are being investigated in emerging studies, of which one has recently reported unfavourable efficacy results associated with the aspirin-free approach compared with conventional DAPT. Finally, $P2Y_{12}$ inhibitor alone has been compared with aspirin alone as chronic therapy after DAPT discontinuation, thus challenging the historical role of aspirin as a standard of care for secondary prevention following PCI. A thorough understanding of study designs, populations, treatments, results, and limitations of trials testing $P2Y_{12}$ inhibitor monotherapy vs. DAPT or vs. aspirin is required to consider adopting this treatment in clinical practice. This review addresses the use of aspirin-free antiplatelet strategies among patients undergoing PCI without a concomitant indication for OAC, providing an overview of clinical evidence, guideline indications, practical implications, ongoing issues, and future perspectives.

Keywords Aspirin-free approaches • $P2Y_{12}$ inhibitor monotherapy • Ticagrelor monotherapy • Clopidogrel monotherapy • Dual antiplatelet therapy

Introduction

Dual antiplatelet therapy (DAPT) with aspirin and an inhibitor of the platelet $P2Y_{12}$ receptor is the treatment of choice after percutaneous coronary interventions (PCI).[1,2] The indication for DAPT after PCI derives from placebo-controlled studies showing the benefit of adding clopidogrel to aspirin.[3] Additionally, the superior clinical efficacy of prasugrel and ticagrelor vs. clopidogrel has been shown on a background of aspirin therapy.[4,5] These studies have provided the evidence for DAPT after PCI (i.e. adding a $P2Y_{12}$ inhibitor to aspirin) for a variable period followed by lifelong aspirin monotherapy.[1,2]

Dual antiplatelet therapy after PCI reduces ischaemic events at the expense of increased bleeding. The transition from short DAPT to $P2Y_{12}$ inhibitor monotherapy has recently gained popularity as a strategy to reduce aspirin-related bleeding while preserving the antithrombotic benefit of DAPT.[6] The assumption that the efficacy of $P2Y_{12}$ inhibitor monotherapy could be comparable with that of DAPT is based on evidence that aspirin does not substantially decrease platelet reactivity when added to more potent $P2Y_{12}$ inhibition.[7–9] This hypothesis is being tested in randomized clinical trials (RCTs) comparing standard-duration DAPT vs. the $P2Y_{12}$ inhibitor monotherapy started immediately after PCI or following a short-course DAPT after PCI among patients without a concomitant indication for oral anticoagulation (OAC) (*Graphical Abstract*). The effect of aspirin withdrawal has also been assessed in RCTs comparing the dual combination of the $P2Y_{12}$ inhibitor with OAC vs. triple antithrombotic therapy with DAPT plus OAC in patients undergoing PCI with concomitant indication to OAC. Moreover, the consideration that the historical role of aspirin for secondary prevention is based on outdated studies preceding the use of more effective strategies[10,11] has prompted the reassessment of the relative effect of aspirin vs. the $P2Y_{12}$ inhibitor as chronic antithrombotic monotherapy.

The present review addresses the use of aspirin-free antiplatelet strategies in patients undergoing PCI without a concomitant indication for OAC, providing an overview of clinical evidence, practical implications, ongoing issues, and future perspectives.

$P2Y_{12}$ inhibitor monotherapy vs. dual antiplatelet therapy

Several studies compared standard DAPT with the aspirin-free regimen of $P2Y_{12}$ inhibitor monotherapy (ticagrelor or clopidogrel) following short DAPT (1–3 months) after PCI. Two recent trials compared standard DAPT with the $P2Y_{12}$ inhibitor monotherapy following a shorter DAPT period (<1 month) after PCI or started immediately at PCI time. On the other hand, one study compared DAPT with clopidogrel monotherapy in the chronic phase post-PCI after standard-duration DAPT (9–12 months) in high-risk patients who may benefit from prolonged DAPT. Details of these studies are provided below.

Ticagrelor monotherapy following dual antiplatelet therapy

The design and results of RCTs comparing ticagrelor monotherapy after short DAPT vs. 12-month DAPT after PCI are summarized in *Figure 1*.[12–16] GLOBAL LEADERS was an open-label, all-comer, PCI trial ($n = 15\,968$) testing ticagrelor monotherapy following 1-month DAPT vs. 12-month DAPT with aspirin plus clopidogrel in chronic coronary syndromes (CCS) or aspirin plus ticagrelor in acute coronary syndromes (ACS), followed by aspirin alone for additional 12 months.[12] The 2-year primary endpoint of all-cause death or non-fatal Q-wave myocardial infarction (MI) was not significantly different between the two groups, and no significant reductions in all-cause mortality and Q-wave MI were observed. Major or minor bleeding was similar. In the GLASSY ancillary study including patients ($n = 7585$) from the 20 top-recruiting sites with centrally adjudicated events, ticagrelor monotherapy was non-inferior, but not superior, to standard DAPT for the 2-year endpoint of all-cause death, non-fatal MI, non-fatal stroke, or urgent target vessel revascularization, without significant differences in bleeding.[13] These results suggest no significant benefit but also no harm of ticagrelor monotherapy vs. 12-month DAPT followed by aspirin in a heterogeneous PCI population.

In a double-blind manner, the TWILIGHT trial tested the superiority of ticagrelor monotherapy over DAPT with respect to major or

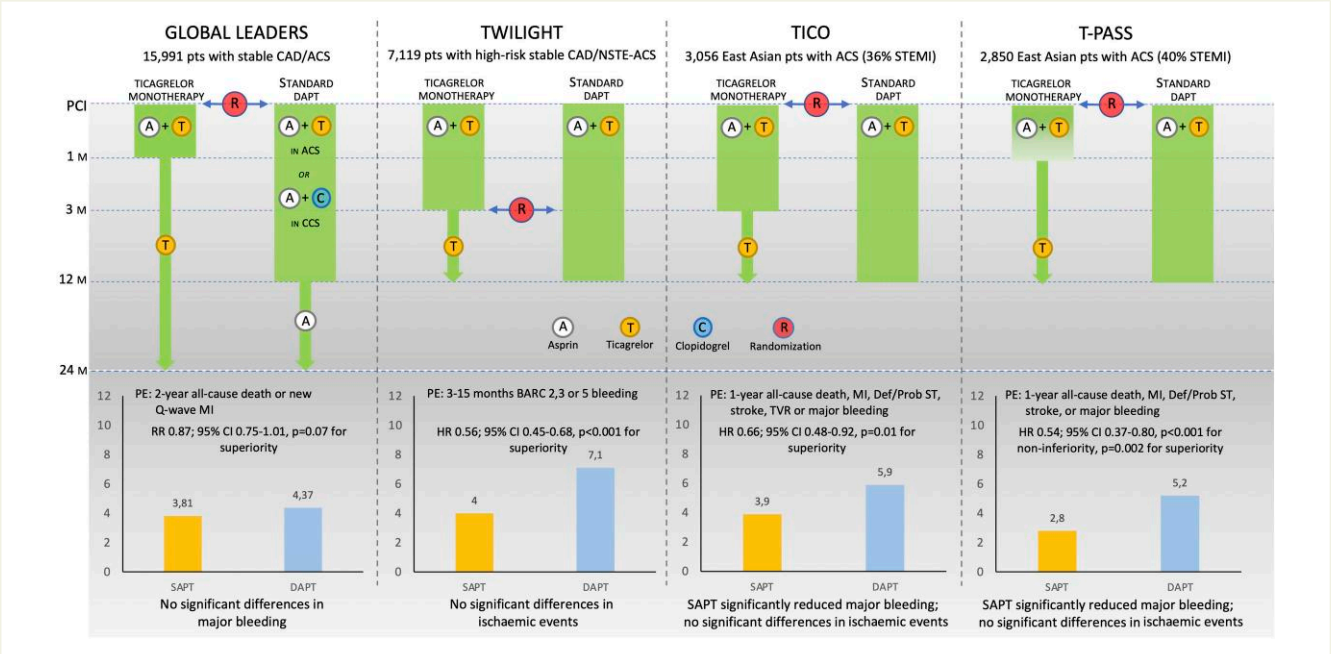

Figure 1 Design and results of randomized studies on ticagrelor monotherapy vs. DAPT. ACS, acute coronary syndrome; BARC, Bleeding Academic Research Consortium; CAD, coronary artery disease; CI, confidence interval; DAPT, dual antiplatelet therapy; HR, hazard ratio, MI, myocardial infarction; NSTE-ACS, non–ST-elevation acute coronary syndrome; PE, primary endpoint; R, randomization; RR, rate ratio; SAPT, single antiplatelet therapy; ST, stent thrombosis; STEMI, ST-elevation myocardial infarction; TVR, target vessel revascularization

clinically relevant non-major bleeding in PCI patients ($n = 7119$) who were event-free at 3 months after DAPT and were at high risk for bleeding or an ischaemic event.[14] At 1 year after randomization, ticagrelor monotherapy provided substantial relative reductions of 44% and 51% in the primary bleeding endpoint and in major bleeding, respectively, while being non-inferior to DAPT regarding the efficacy endpoint (all-cause death, non-fatal MI, or non-fatal stroke).

Finally, the TICO trial, including 3056 ACS patients treated with PCI in South Korea, found a 1-year net clinical endpoint to be significantly reduced by 3-month DAPT followed by ticagrelor monotherapy vs. 12-month DAPT, driven by lower rates of major bleeding [1.7% vs. 3.0%; hazard ratio (HR) 0.56, 95% confidence interval (CI) 0.34–0.91, $P = .02$] and no significant differences in ischaemic events.[15]

Those three RCTs showed similar or better net outcomes with ticagrelor alone following a short-course DAPT of at least 1 month after PCI (i.e. an aspirin-free strategy) vs. standard-duration DAPT. Consistent results were observed in the open-label T-PASS trial showing that among ACS patients ($n = 2850$) from South Korea ticagrelor monotherapy following aspirin withdrawal within 1 month (median 16 days) was non-inferior and superior to 12-month DAPT for the net composite endpoint, driven by significant reduction in major bleeding (1.2% vs. 3.4%; HR 0.35, 95% CI 0.20–0.61, $P < .001$).[16]

Clopidogrel monotherapy following dual antiplatelet therapy

The design and results of key trials assessing short DAPT (1–3 months) followed by mostly clopidogrel monotherapy vs. 12-month DAPT in patients undergoing PCI without concomitant indication to an OAC are summarized in *Figure 2*.[17–19] These RCTs solely included East Asian populations. In the SMART-CHOICE open-label trial ($n = 2993$), 3-month DAPT followed by mostly clopidogrel monotherapy was non-inferior to 12-month DAPT regarding the 1-year primary composite endpoint of ischaemic events, and it significantly reduced bleeding.[17] The relatively wide non-inferiority margin limits the study power for ischaemic events.

The STOPDAPT-2 open-label trial showed that among 3045 Japanese patients undergoing PCI guided by intracoronary imaging (99.7%), clopidogrel monotherapy was superior to 12-month DAPT for a 1-year net composite endpoint, driven by reduction in overall bleeding with no significant differences in ischaemic events.[18] However, these results could be affected by the lower-than-expected primary endpoint event rate, the very low power for ischaemic events, the selective enrolment of low-risk patients, and limited applicability of the findings given the low use of intravascular imaging in routine practice.

The STOPDAPT-2 ACS RCT included the ACS patients enrolled in the STOPDAPT-2 and newly randomized patients to reach a final ACS population of 4136 patients.[19] At 1 year, clopidogrel monotherapy following 1- or 2-month DAPT failed to meet non-inferiority to 12-month DAPT for the net composite endpoint of cardiovascular and bleeding events, due to a numerical increase in MI, highlighting the importance of accurate selection of the $P2Y_{12}$ inhibitor monotherapy after short DAPT in ACS patients. Nevertheless, the lower-than-anticipated rate of the primary endpoint renders the trial underpowered.

Clopidogrel monotherapy was also compared with extended DAPT during the chronic phase post-PCI in the OPT-BIRISK trial.[20] Among Chinese patients ($n = 7758$) with both high bleeding and ischaemic risk who had completed 9–12 months DAPT post-PCI for ACS, clopidogrel monotherapy was superior to DAPT in reducing the primary

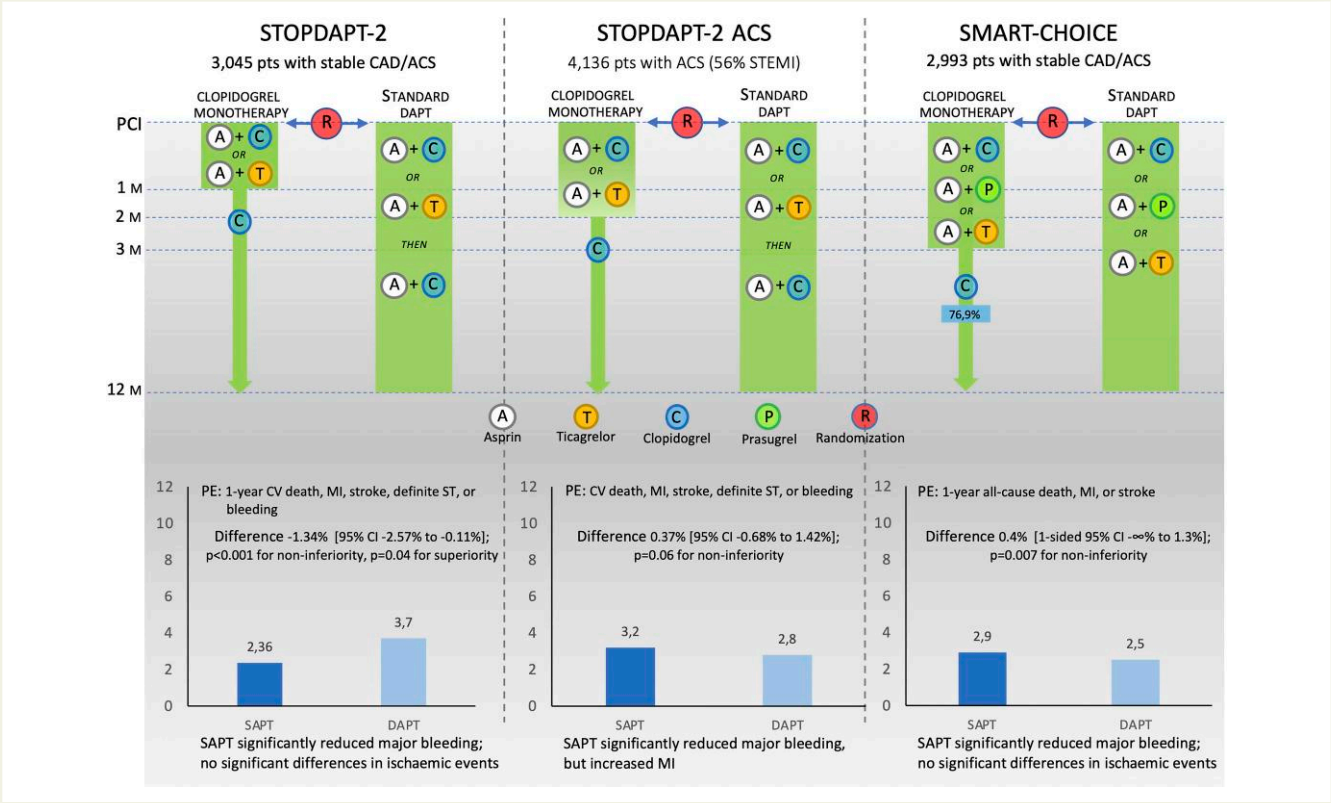

Figure 2 Design and results of randomized studies on clopidogrel monotherapy vs. DAPT. ACS, acute coronary syndrome; CAD, coronary artery disease; CI, confidence interval; CV, cardiovascular; DAPT, dual antiplatelet therapy; HR, hazard ratio, MI, myocardial infarction; PE, primary endpoint; R, randomization; SAPT, single antiplatelet therapy; ST, stent thrombosis; STEMI, ST-elevation myocardial infarction

endpoint of Bleeding Academic Research Consortium (BARC) ≥ 2 bleeding at 9 months (2.5% vs. 3.3%, HR 0.75, 95% CI 0.57–0.97, $P = .03$). Also, rates of ischaemic events were lower with clopidogrel monotherapy (Yaling Han, unpublished data).

Finally, an aspirin-free approach, mostly using clopidogrel monotherapy, was assessed in several trials in PCI patients with a concomitant indication for OAC, showing a superior safety and similar efficacy of the dual ($P2Y_{12}$ inhibitor plus OAC) vs. triple (DAPT plus OAC) antithrombotic therapy.[21] Details of these trials are not provided as they go beyond the scope of the present review.

$P2Y_{12}$ inhibitor monotherapy without initial dual antiplatelet therapy or after very short dual antiplatelet therapy

The hypothesis that monotherapy with a potent $P2Y_{12}$ inhibitor started immediately from PCI may reduce bleeding while preserving efficacy compared with traditional DAPT was tested in the STOPDAPT-3 trial.[22] Among Japanese patients ($n = 6002$) with ACS or high bleeding risk (HBR), the aspirin-free strategy using low-dose prasugrel (20 mg/3.75 mg) started at the time of PCI failed to reduce 30-day major bleeding compared with DAPT and increased 1-month stent thrombosis and unplanned coronary revascularization. These results mitigated the positive preliminary feasibility findings from pilot studies showing no overt safety concerns with ticagrelor or prasugrel monotherapy following aspirin withdrawal immediately after PCI in low-risk patients.[23–26] The MACT study showed that among ACS patients ($n = 200$), the withdrawal of aspirin and addition of low-dose colchicine (0.6 mg daily) to ticagrelor or prasugrel on the day after PCI was safe and associated with favourable platelet function and inflammatory profiles.[26]

$P2Y_{12}$ inhibitor monotherapy vs. dual antiplatelet therapy in higher-risk subgroups

Acute coronary syndrome

The results of some trials testing $P2Y_{12}$ inhibitor monotherapy may have been affected by the mixed inclusion of patients with ACS and CCS since they have differing risks of ischaemic and bleeding events. Only TICO, T-PASS and STOPDAPT-2 ACS exclusively included ACS patients.[15,16,19] Compared with DAPT, clopidogrel monotherapy tended to increase the ischaemic risk in STOPTDAP-2 ACS, while ticagrelor monotherapy showed similar anti-ischaemic efficacy in the overall ACS populations and in high-risk subgroups [e.g. diabetic and ST-elevation MI (STEMI)].[27,28] However, the specific population ethnicity, the use of a composite net clinical endpoint, and the lower-than-expected event rate may limit the generalizability and internal validity of TICO and T-PASS results. Nevertheless, the favourable profile of ticagrelor monotherapy among ACS patients was also shown in GLOBAL LEADERS and TWILIGHT trial subgroup analyses.[29,30] Different from results observed in the overall GLOBAL LEADERS population, a landmark analysis between 31 and 365 days after randomization among ACS patients ($n = 7487$, of whom only 28% with STEMI) showed that ticagrelor monotherapy significantly reduced the relative risk of major bleeding by 48% vs. ticagrelor-based DAPT and numerically reduced the risk of death or Q-wave MI.[29]

Moreover, ticagrelor monotherapy significantly reduced the 2-year risk of major bleeding among ACS patients but not among patients with CCS.[30] Lastly, in TWILIGHT subgroup analysis, compared with DAPT, ticagrelor monotherapy markedly reduced bleeding by 53% among patients with non–ST-elevation ACS and by 24% in stable patients.[31] Rates of efficacy endpoints were similar between groups regardless of clinical presentation. These results suggest that the clinical benefits of ticagrelor monotherapy after a short period of DAPT are preserved and even relatively enhanced among ACS patients, plausibly due to their higher bleeding risk than CCS patients. However, future dedicated studies in ACS populations including patients at higher risk are needed to confirm these subgroup results.

Complex percutaneous coronary interventions

Several trials' subgroup studies and meta-analyses have shown no increase in ischaemic events and reduced bleeding with 1–3-month DAPT followed by $P2Y_{12}$ inhibitor monotherapy vs. 12-month DAPT among patients with complex PCI.[32–37] In an individual patient-level meta-analysis including 22 941 patients from GLASSY, SMART-CHOICE, STOPDAPT-2, TICO, and TWILIGHT trials, those with complex PCI ($n = 4685$) represented only 20.4%.[36] The primary endpoint, combining all-cause mortality, MI, and stroke, was similar between $P2Y_{12}$ inhibitor monotherapy and DAPT among patients with complex PCI (3.61% vs. 4.10%; HR 0.87, 95% CI 0.64–1.19) and those with non-complex PCI (2.75% vs. 3.21%; HR 0.91, 95% CI 0.76–1.09). $P2Y_{12}$ inhibitor monotherapy reduced major bleeding regardless of PCI complexity. However, these positive results should be interpreted considering specific characteristics of patients with complex PCI including ~37% from East Asia, 39% presenting with a CCS, and only a small proportion having a STEMI ($n = 553$). Therefore, future studies on $P2Y_{12}$ inhibitor monotherapy including more complex patients are needed to confirm currently available exploratory results.

High bleeding risk

The results of post-hoc analyses of patients with HBR from RCTs comparing the $P2Y_{12}$ inhibitor monotherapy approach after short DAPT vs. standard DAPT are summarized in *Table 1*.[38–41] Overall, the reduction in bleeding without increase in composite ischaemic events was consistent irrespective of HBR status, but the magnitude of the effect was more pronounced among HBR patients. A recent study-level meta-analysis pooled data on HBR patients from trials of $P2Y_{12}$ inhibitor monotherapy vs. standard DAPT and from trials with short (≤3 months) vs. standard (≥6 months) DAPT in which aspirin monotherapy has also been used after DAPT interruption in the short regimen arm.[42] Among 9006 HBR patients undergoing PCI from 11 trials, short DAPT was associated with significantly reduced major or clinically relevant non-major bleeding and cardiovascular mortality while providing similar rates of ischaemic events.

Meta-analyses on $P2Y_{12}$ inhibitor monotherapy vs. dual antiplatelet therapy

Study-level meta-analyses including GLOBAL LEADERS, SMART-CHOICE, STOPDAPT-2, TWILIGHT, and TICO trials have confirmed that withdrawal of aspirin from DAPT at 1–3 months after PCI is associated with significant reduction in bleeding without increasing individual ischaemic events, regardless of clinical presentation.[43,44] In the Sidney-2 Collaboration including patient-level data from 24 096 participants in six trials (GLASSY, SMART-CHOICE, STOPDAPT-2, TWILIGHT, and TICO plus the DACAB trial comparing ticagrelor with or without aspirin vs. aspirin monotherapy for bypass graft patency), the $P2Y_{12}$ inhibitor monotherapy strategy was non-inferior to DAPT considering the combination of death, stroke, or MI (HR 0.93, 95% CI 0.79–1.09, $P = .005$), without differences in individual ischaemic events and significant reduction in bleeding.[45] These results were consistent in patients with ACS. Another individual patient-level meta-analysis including GLASSY and TWILIGHT trials ($n = 14\,628$) showed reduced rates of major bleeding and death with ticagrelor monotherapy vs. DAPT, without significant difference in overall ischaemic events.[46] These meta-analyses, which do not include data from the STOPDAPT-2 ACS trial, provide further support to the beneficial effect of $P2Y_{12}$ inhibitor monotherapy following short DAPT after PCI, as shown in individual trials.

Mechanistic explanations for the clinical effects of the $P2Y_{12}$ inhibitor monotherapy vs. dual antiplatelet therapy

Potential mechanistic insights for findings of clinical trials assessing the $P2Y_{12}$ inhibitor monotherapy have been explored in dedicated pharmacodynamic studies on ticagrelor monotherapy.[47–49] In the TWILIGHT platelet substudy, platelet reactivity was similar with ticagrelor monotherapy vs. DAPT when adenosine diphosphate and thrombin were used as stimuli for platelet aggregation.[47] Conversely, platelet reactivity after arachidonic acid and collagen, which are markers sensitive to cyclo-oxygenase-1 (COX-1) blockade, was higher with ticagrelor monotherapy. Importantly, the two treatments provided a similar antithrombotic effect measured by the area of platelet-rich thrombus formed under dynamic flow conditions, suggesting that ticagrelor monotherapy provides sufficient blockade of the key pathways of thrombus formation. Consistent results were observed in the GLOBAL LEADERS platelet substudy, showing that following aspirin withdrawal at 1 month, platelet aggregation increased in response to arachidonic acid and collagen.[48] Finally, the TEMPLATE randomized study ($n = 110$) showed that at 4 weeks after PCI, platelet aggregation was similar with ticagrelor monotherapy and DAPT after stimulation with thrombin receptor activation peptide-6 and a thromboxane A_2 receptor agonist, while it was higher with ticagrelor in response to the collagen-related peptide stimulating the glycoprotein VI receptor.[49] This latter difference may not explain by itself the reduction in bleeding with ticagrelor monotherapy vs. DAPT, due to the modest role played in haemostasis by the glycoprotein VI receptor.[50] In general, the effects of ticagrelor monotherapy may be attributed to the fact that this treatment compared with DAPT similarly inhibits most platelet activation pathways while it is not sufficient to suppress platelet reactivity to COX-1–sensitive agonists, which may hypothetically allow for a platelet reactivity attenuation sufficient to improve haemostasis without relevantly impacting on thrombosis. However, the exact mechanisms underlying results of trials on $P2Y_{12}$ inhibitor monotherapy vs. DAPT remain uncertain.

The pharmacodynamic effects observed with ticagrelor monotherapy may not occur with clopidogrel. Indeed, a study has shown that aspirin withdrawal from a background therapy with clopidogrel and vorapaxar was associated with an increase in markers of $P2Y_{12}$-mediated platelet reactivity, most likely due to the greater variability and lower intensity of clopidogrel inhibitory effects.[51]

Studies on $P2Y_{12}$ inhibitor vs. aspirin post-percutaneous coronary interventions

Most studies on $P2Y_{12}$ inhibitor monotherapy have used DAPT as a control group, with few investigations directly comparing $P2Y_{12}$

Table 1 Outcomes according to high bleeding risk status in trials of $P2Y_{12}$ inhibitor monotherapy vs. dual antiplatelet therapy after percutaneous coronary interventions

Trial	HBR patients	Non-HBR patients	HBR definition	Results
GLOBAL LEADERS	$n = 2483$ (16.6%)	12 445 (83.4%)	PD score ≥ 25	Outcomes according to HBR status were not reported.
TWILIGHT	$n = 1064$ (17.2%)	$n = 5\,114$[a] (82.8%)	ARC-HBR	The primary endpoint of BARC bleeding 2, 3, and 5 was reduced with ticagrelor monotherapy vs. DAPT in: • HBR (6.3% vs. 11.4%; HR 0.53, 95% CI 0.35–0.82) • Non-HBR (3.5% vs. 5.9%; HR 0.59, 95% CI 0.46–0.77) Greater ARD in HBR (−5.1% vs. −2.3%; difference in ARDs −2.8%, 95% CI −6.4% to 0.8%, $P = .130$). No significant difference in death, MI, or stroke between arms, irrespective of HBR status.
TICO	$n = 453$[a] (15.2%)	$n = 2\,527$[a] (84.8%)	ARC-HBR and PD score ≥ 25	Based on the ARC-HRC definition[b], the 3–12-month primary endpoint of NACE was reduced with ticagrelor monotherapy vs. DAPT in: • HBR (2.4% vs. 8.0%; HR 0.30, 95% CI 0.11–0.80) • Non-HBR (1.3% vs. 2.6%; HR 0.49, 95% CI 0.27–0.89) Major bleeding was reduced with ticagrelor monotherapy vs. DAPT in: • HBR (0.5% vs. 4.7%; HR 0.10, 95% CI 0.01–0.81) • Non-HBR (0.2% vs. 1.0%; HR 0.16, 95% CI 0.04–0.73) No difference in ischaemic events, irrespective of HBR status.
STOPDAPT-2 Total Cohort	$n = 1893$ (31.6%)	$n = 4104$ (68.4%)	ARC-HBR	The 1-year primary endpoint of NACE was not significantly different between clopidogrel monotherapy vs. DAPT in HBR and non-HBR. Major/minor bleeding was reduced with clopidogrel monotherapy vs. DAPT in: • HBR (0.66% vs. 2.27%; HR 0.29, 95% CI 0.12–0.72) • Non-HBR (0.43% vs. 0.85%; HR 0.51, 95% CI 0.23–1.15) Clopidogrel monotherapy vs. DAPT was associated with a numerical increase in MI among HBR patients (2.01% vs. 0.62%).

ARC-HBR, Academic Research Consortium criteria for HBR; ARD, absolute risk difference; BARC, Bleeding Academic Research Consortium; CI, confidence interval; DAPT, dual antiplatelet therapy; HBR, high bleeding risk; HR, hazard ratio; MI, myocardial infarction; NACE, net adverse clinical events; PD, PRECISE-DAPT.
[a]This TICO analysis was based on a total of 2980 patients without adverse events during the first 3 months after PCI: 453 were HBR by ARC-HBR, and 504 were HBR by PRECISE-DAPT score.
[b]Results were consistent with HBR definition based on PRECISE-DAPT ≥ 25.

inhibitor and aspirin following a variable DAPT period after PCI (*Table 2*). The HOST-EXAM is the only RCT available directly comparing aspirin vs. clopidogrel following 6–18 months DAPT after PCI.[52] Among 5438 patients from South Korea clopidogrel (vs. aspirin) provided a significant 27% relative reduction in the 2-year primary net clinical endpoint, mostly driven by significant reductions in bleeding, stroke, and readmission for ACS. A non-significant numerical increase in non-cardiovascular death (particularly cancer-related death) was observed with clopidogrel at 24 months. The HOST-EXAM Extended Study showed that at long term, clopidogrel monotherapy maintained a consistent 26% relative reduction in the primary net endpoint with similar rates of all-cause death between groups.[53] While striking, the results of the HOST-EXAM trial should be interpreted in the context of the unique characteristics of the East Asian patients who carry a higher prevalence of cytochrome mutations causing an attenuated antiplatelet effect of clopidogrel.[54,55] However, the lower thrombotic event rates reported in East Asian vs. White populations would imply that the prognostic value of a decreased clopidogrel response might be different between ethnicities, thus limiting the generalizability of the HOST-EXAM trial results.[56] Moreover, the open-label design of the trial, along with the lower-than-anticipated rate of the primary endpoint, may warrant some notes of caution.[57]

Another direct comparison between $P2Y_{12}$ inhibitor or aspirin monotherapy after PCI has been performed in a GLOBAL LEADERS landmark analysis reporting on the second year after PCI when patients were on monotherapy with ticagrelor or aspirin.[58] This analysis showed that patients ($n = 11\,121$) who were free of events during the first year after PCI and adherent to their assigned therapy had a lower risk of MI and numerically higher bleeding rates with ticagrelor vs. aspirin (*Table 2*). However, the number needed to treat (NNT) to prevent a MI was high, arguing against the routine use of ticagrelor vs. aspirin beyond the first year after PCI.

The two monotherapies were tested head-to-head in an indirect comparison between the two PCI populations with ACS treated with $P2Y_{12}$ inhibitor monotherapy after 3-month DAPT and with aspirin monotherapy after 6-month DAPT from the SMART-CHOICE and SMART-DATE RCTs, respectively.[59] Compared with aspirin, the $P2Y_{12}$ inhibitor monotherapy tended to significantly reduce the risk of MI and bleeding. However, these results should be interpreted with caution due to inherent limitations of indirect comparisons and low event rates.

Table 2 Trials directly comparing $P2Y_{12}$ inhibitor vs. aspirin after percutaneous coronary interventions

Study	*n* of Patients	Study design	Clinical setting	Treatment arms	Endpoints
HOST-EXAM	$n = 5438$	Randomized, open-label trial	Post-PCI: 6–18 months	Clopidogrel vs. aspirin	All-cause death, non-fatal MI, stroke, readmission due to ACS, and BARC ≥ 3 (primary endpoint): • 5.7% vs. 7.7%; HR 0.73, 95% CI 0.59–0.90, $P = .0035$, at 24 months (NNT 51) • 12.8% vs. 16.9%; HR 0.74, 95% CI 0.63–0.86, $P < .001$, at a median of 5.8 years (NNT 24) All-cause death: • 1.9% vs. 1.3%; HR 1.43, 95% CI 0.93–2.19, $P = .101$, at 24 months • 6.2% vs. 6.0; HR 1.04, 95% CI 0.82–1.31, $P = .74$, at a median of 5.8 years BARC ≥ 3: • 1.2% vs. 2.0%; HR 0.63, 95% CI 0.41–0.97, $P = .035$, at 24 months (NNT 125) • 2.6% vs. 3.9%; HR 0.65, 95% CI 0.47–0.90, $P = .008$, at a median of 5.8 years (NNT 77) Stroke and readmission due to ACS were significantly reduced with clopidogrel, while no significant reduction in MI was observed at both 24 months and long-term follow-up.
GLOBAL LEADERS landmark analysis	$n = 11\,121$	Subanalysis from a randomized open-label trial	Post-PCI: 12 months	Ticagrelor vs. aspirin	All-cause death, any MI, and any stroke: • 1.9% vs. 2.6%; adjusted HR 0.74; 95% CI 0.58–0.96, $P = .02$, between 12 and 24 months after PCI (NNT 145) Any MI: • 0.7% vs. 1.2%; adjusted HR 0.54; 95% CI 0.36–0.82, $P = .003$, between 12 and 24 months after PCI (NNT 189) BARC 3 or 5 bleeding: • 0.5% vs. 0.3%; adjusted HR 1.89; 95% CI 1.03–3.45, $P = .005$, between 12 and 24 months after PCI (NNT −417) No significant differences in all-cause death and stroke were observed.

ACS, acute coronary syndrome; BARC, Bleeding Academic Research Consortium; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; NNT, number needed to treat; PCI, percutaneous coronary intervention.

Meta-analysis on $P2Y_{12}$ inhibitor vs. aspirin post-percutaneous coronary interventions

A network meta-analysis has compared the $P2Y_{12}$ inhibitor vs. aspirin following DAPT discontinuation after PCI by pooling the direct evidence from HOST-EXAM trial and GLOBAL LEADERS subanalysis with the indirect evidence from RCTs separately comparing conventional DAPT with the $P2Y_{12}$ inhibitor or aspirin monotherapies following short DAPT.[60] Among patients ($n = 73\,126$) undergoing PCI from 19 trials, aspirin was associated with a significant 32% relative increase in MI and similar bleeding compared with $P2Y_{12}$ inhibitor monotherapy. No significant differences in death, stroke, and stent thrombosis were observed between the two monotherapies. The NNT for $P2Y_{12}$ inhibitor to prevent one MI was 261 in the overall analysis and 155 when only direct evidence was considered, suggesting a potentially more relevant benefit when homogenous populations are compared.

Similar results were reported in other meta-analyses comparing the $P2Y_{12}$ inhibitor vs. aspirin monotherapy in the setting of secondary prevention in patients with atherosclerotic disease.[61–63] Among these latter, the PANTHER was the only individual patient-level meta-analysis focusing on patients ($n = 24\,325$) with coronary artery disease (CAD) from two trials assessing the two monotherapies at 6–18 months post-PCI (GLASSY, HOST-EXAM), two trials on patients at 24 h after cardiac surgery (DACAB and TiCAB), and three trials on patients with stable CAD and recent or previous MI (ASCET, CADET, and CAPRIE).[61] Among patients ($n = 12\,178$) assigned to $P2Y_{12}$ inhibitor monotherapy, mostly clopidogrel (62.0%), the 2-year primary endpoint of cardiovascular death, MI, and stroke was lower compared with that of those ($n = 12\,147$) assigned to aspirin, mainly owing to reduction in MI (NNT 136). Major bleeding was similar between the two monotherapies. These overall positive results might be mitigated by the fact that included studies on stable CAD or prior MI were performed in an era preceding current cardiovascular prevention strategies.[64] Moreover, the PANTHER findings appear relevantly

impacted by the HOST-EXAM, thus somehow carrying same trial limitations.

An important observation of these meta-analyses is the overall similar bleeding between the two monotherapies. However, risk of gastrointestinal bleeding was not assessed. The potential for a higher risk of gastrointestinal bleeding with clopidogrel has been challenged in the OPT-PEACE study showing that aspirin and clopidogrel had similar effects on gastrointestinal mucosal injury.[65] Even though this study included a small number of patients ($n = 505$) with low bleeding risk, its reported findings add to the uncertainty surrounding the relative effect on bleeding of the two monotherapies.

Selection of the $P2Y_{12}$ inhibitor monotherapy

Based on the accruing evidence on $P2Y_{12}$ inhibitor monotherapy, the 2021 American and 2020 European guidelines have introduced the indication that a regimen of short DAPT followed by the $P2Y_{12}$ inhibitor monotherapy should be considered in selected patients undergoing PCI.[1,66] Following these guidelines, an international consensus document has suggested that the regimen of 1–3 months DAPT followed by $P2Y_{12}$ inhibitor monotherapy should be the default strategy, with the use of conventional/prolonged DAPT restricted only to patients at high ischaemic risk and very low bleeding risk.[67,68] However, the recent 2023 American and European guidelines have confirmed that 6- and 12-month DAPT is the default strategy in patients undergoing PCI for stable CAD or ACS, respectively, while the $P2Y_{12}$ inhibitor monotherapy after short DAPT should be considered in selected patients to reduce bleeding (*Table 3*).[69,70] The 2023 European guidelines on ACS indicate that monotherapy (preferably with a $P2Y_{12}$ inhibitor) should be considered after event-free short DAPT (3–6 months) in patients without high ischaemic risk (*Table 3*). Also, these guidelines recommend that 1-month DAPT followed by aspirin or $P2Y_{12}$ inhibitor monotherapy may be considered. Based on these indications, a practical personalized selection process of the $P2Y_{12}$ inhibitor monotherapy following short DAPT after PCI is proposed in *Figure 3*, showing possible antithrombotic options according to the HBR status.

In patients without HBR, standard-duration DAPT is the treatment of choice, while the regimen of short DAPT followed by the $P2Y_{12}$ inhibitor should be considered an alternative to DAPT in patients without high ischaemic risk to avoid unnecessary exposure to DAPT. This approach is based on some considerations regarding landmark trials comparing $P2Y_{12}$ inhibitor monotherapy with DAPT. Most of those trials have tested superiority for the net composite endpoint or non-inferiority for overall ischaemic events, reducing the power for detecting differences in individual thrombotic and ischaemic endpoints. Despite several meta-analyses having confirmed the reduction in bleeding and no differences in ischaemic events with $P2Y_{12}$ inhibitor monotherapy vs. DAPT, those pooled data carry limitations of individual studies.[43–46] Indeed, as discussed above, most patients included in landmark studies of $P2Y_{12}$ inhibitor monotherapy were at low-to-intermediate ischaemic risk limiting the strength of positive results observed among more complex patients. In patients with HBR, increasing evidence supports the use of short DAPT (1–3 months).[42,71] In this regard, the regimen of short DAPT followed by the $P2Y_{12}$ inhibitor monotherapy appears to represent a reasonable choice that should be used as default strategy in HBR patients with low-to-moderate ischaemic risk and as an alternative to standard DAPT in those with concomitant high ischaemic risk based on the balance between the two risks.

Aspirin could also be considered as monotherapy after short DAPT (*Table 3*).[1,70] No trial has compared short-term DAPT followed by $P2Y_{12}$ inhibitor or by aspirin monotherapy. In several RCTs, this latter regimen has been associated with reduced bleeding without excess in overall ischaemic events compared with standard DAPT.[72] However, aspirin monotherapy after PCI has been investigated mostly starting from a DAPT period of 6 months onwards among patients with low ischaemic risk.[72–75] Also, among ACS patients, aspirin monotherapy after short DAPT was associated with a trend towards a greater risk of MI than DAPT.[76–78] The higher risk of MI with aspirin was also observed vs. $P2Y_{12}$ monotherapy in indirect comparisons.[53] Based on these considerations, it is reasonable to consider aspirin monotherapy after short DAPT only in HBR patients who are deemed not at high ischaemic risk.

The optimal antiplatelet monotherapy after discontinuation of standard-duration DAPT and for long-term secondary prevention is a currently debated issue. In this context, emerging studies have shown a superior efficacy and similar safety of $P2Y_{12}$ inhibitor vs. aspirin monotherapy.[52,53,58–61] However, as described above, these studies include mainly non-randomized comparisons and carry several limitations leading current European guidelines on ACS to provide a Class IIb for the long-term treatment with $P2Y_{12}$ inhibitor monotherapy as an alternative to aspirin.[70]

Finally, beside the DAPT shortening strategy followed by aspirin or the $P2Y_{12}$ inhibitor, another DAPT de-escalation strategy consists in switching from prasugrel or ticagrelor to clopidogrel early after PCI (*Table 3*), which has been associated with decreased bleeding and overall ischaemic events compared with standard DAPT.[79,80] An indirect network meta-analysis showed that the $P2Y_{12}$ inhibitor de-escalation vs. short DAPT followed by aspirin or $P2Y_{12}$ inhibitor monotherapy is associated with decreased net clinical events,[81] supporting $P2Y_{12}$ inhibitor de-escalation as a possible alternative to short DAPT in selected patients with ACS who are deemed unsuitable for more potent $P2Y_{12}$ inhibitors.

Practical issues related to $P2Y_{12}$ inhibitor monotherapy

The choice of a regimen of short DAPT followed by $P2Y_{12}$ inhibitor monotherapy raises some practical issues. First, the $P2Y_{12}$ inhibitors used as monotherapy across studies were mostly ticagrelor or clopidogrel raising the question on which agent should be selected. European guidelines recommend that prasugrel should be considered in preference to ticagrelor for ACS patients who proceed to PCI (Class IIa), yet data on prasugrel monotherapy are still limited.[70] Based on the STOPDAPT-2 ACS trial results, clopidogrel does not appear a viable option following 1-month DAPT after PCI in ACS patients. Instead, clopidogrel is the agent of choice when the regimen of short DAPT followed by $P2Y_{12}$ monotherapy is used in CCS patients without HBR and with low ischaemic risk (*Figure 3*). In CCS patients with HBR in whom short DAPT is selected, ticagrelor/prasugrel monotherapy may be preferred over clopidogrel among those with a concomitant high ischaemic risk. Indeed, one of the major concerns with clopidogrel monotherapy is that this strategy may expose patients with on-treatment high platelet reactivity (HPR) to an increased risk of thrombotic events.[82] However, the pharmacodynamic effects of clopidogrel did not translate into an overall increased thrombotic risk among low-risk populations enrolled in trials of clopidogrel monotherapy. In an analysis of the SMART-CHOICE trial, clopidogrel monotherapy and DAPT showed a similar ischaemic risk in patients with or without HPR.[83] Nevertheless, future studies are warranted to assess the clinical

Table 3 Guideline recommendations on dual antiplatelet therapy de-escalation strategies in percutaneous coronary intervention patients without concomitant indication for oral anticoagulation

Scientific societies/year	Clinical setting	Recommendation
ESC 2023	Management of ACS	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 $P2Y_{12}$ receptor inhibitor) should be considered (Class IIa, LoE A). In HBR patients, aspirin or $P2Y_{12}$ receptor inhibitor monotherapy after 1 month of DAPT may be considered (Class IIb, LoE B). De-escalation of $P2Y_{12}$ 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 (Class IIb, LoE A). De-escalation of antiplatelet therapy in the first 30 days after an ACS event is not recommended (Class III, LoE B).
AHA/ACC, 2023	Management of chronic CAD	In selected patients with CCD treated with PCI and a drug-eluting stent who have completed a 1- to 3-month course of DAPT, $P2Y_{12}$ inhibitor monotherapy for at least 12 months is reasonable to reduce bleeding risk (Class IIa, LoE A).
ACC/AHA/SCAI, 2021	CAD revascularization	In selected patients undergoing PCI, a shorter duration (1–3 months) of DAPT is reasonable, with subsequent transition to $P2Y_{12}$ inhibitor monotherapy to reduce the risk of bleeding events (Class IIa, LoE A). In patients with high risk of bleeding or overt bleeding on DAPT, discontinuation of the $P2Y_{12}$ inhibitor after 3 months in CCD and 6 months in ACS may be reasonable (Class IIb).

ACC, American College of Cardiology; ACS, acute coronary syndromes; AHA, American Heart Association; CAD, coronary artery disease; CCD, chronic coronary disease; DAPT; dual antiplatelet therapy; ESC, European Society of Cardiology; HBR: high bleeding risk; LoE, level of evidence; NSTE-ACS, non–ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Interventions.

impact of HPR on the effect of clopidogrel monotherapy following a short-course DAPT vs. continued DAPT in selected PCI patients and to support the role of genetic or functional testing to guide selection of the $P2Y_{12}$ inhibitor monotherapy. Second, the duration of the short DAPT period before the transition to $P2Y_{12}$ inhibitor monotherapy ranged from 1 to 3 months across most trials. In European guidelines, the de-escalation of antiplatelet therapy, including the DAPT shortening strategy, is not recommended in the first 30 days after an ACS,[70] despite emerging studies are challenging this contraindication.[16] Therefore, the timing for DAPT de-escalation by aspirin discontinuation from 1 month onwards after PCI should be selected based on clinical setting and individual patient risk as, for instance, proposed in the algorithm in *Figure 3*. Third, the appropriate duration of the $P2Y_{12}$ inhibitor monotherapy beyond the period investigated in trials remains uncertain. For ticagrelor 90 mg monotherapy, it is uncertain if this regimen should be maintained chronically or if switching to ticagrelor 60 or aspirin or clopidogrel is appropriate. Finally, the $P2Y_{12}$ inhibitor monotherapy use after PCI may raise some concerns on the peri-procedural management of this therapy in case of need for non-elective surgery. If the $P2Y_{12}$ inhibitor should be continued or switched to aspirin before a specific endoscopic or surgical procedure remains uncertain and should be discussed in dedicated guidelines.[84]

Ongoing trials on aspirin-free antiplatelet approaches after percutaneous coronary interventions

The key design features of ongoing RCTs testing aspirin-free approaches in patients undergoing PCI without a baseline indication for OAC are summarized in *Table 4*. Several trials will investigate the $P2Y_{12}$ inhibitor monotherapy after a short period (1–3 months) of DAPT after PCI in ACS patients. Among these trials, BULK-STEMI is investigating ticagrelor monotherapy following 3-month DAPT vs. 12-month DAPT, while another four trials (COMPARE STEMI ONE, ULTIMATE-DAPT, TARGET FIRST, and MATE) will compare $P2Y_{12}$ inhibitor monotherapy after about 1-month DAPT vs. standard DAPT among ACS patients.[85–89] Two trials (NEOMINDSET and LEGACY) are investigating prasugrel and ticagrelor monotherapy after very short DAPT (limited to the peri-PCI period) in ACS patients.[90,91] Alongside those ongoing trials in which monotherapy will be tested early after PCI, the SMART-CHOICE 2 trial will investigate clopidogrel monotherapy vs. prolonged DAPT at 9–12 months after PCI in patients with high ischaemic risk.[92] Finally, the SMART-CHOICE 3 trial is being conducted in East Asia to compare the efficacy of clopidogrel vs. aspirin in patients at high risk for recurrent ischaemic events at ≥12 months after PCI.[93]

Conclusions

Antiplatelet monotherapy with $P2Y_{12}$ inhibitors following short DAPT after PCI has been the focus of several RCTs that, within some study limitations, overall support the use of an aspirin-free strategy as an alternative to standard DAPT for selected patients. Based on current evidence, the $P2Y_{12}$ inhibitor monotherapy following a short DAPT period after PCI could be a reasonable alternative strategy in patients without both high bleeding and ischaemic risks and is an attractive option for patients with HBR. However, uncertainty surrounds the optimal antithrombotic strategy to be selected according to the individual patient risk. Moreover, several practical issues raised by the $P2Y_{12}$ inhibitor monotherapy use will need to be addressed. Finally, questions remain on the role of $P2Y_{12}$ inhibitor monotherapy over aspirin for long-term maintenance after PCI. Ongoing RCTs, which are mostly comparing $P2Y_{12}$ inhibitor monotherapy with or without an initial short

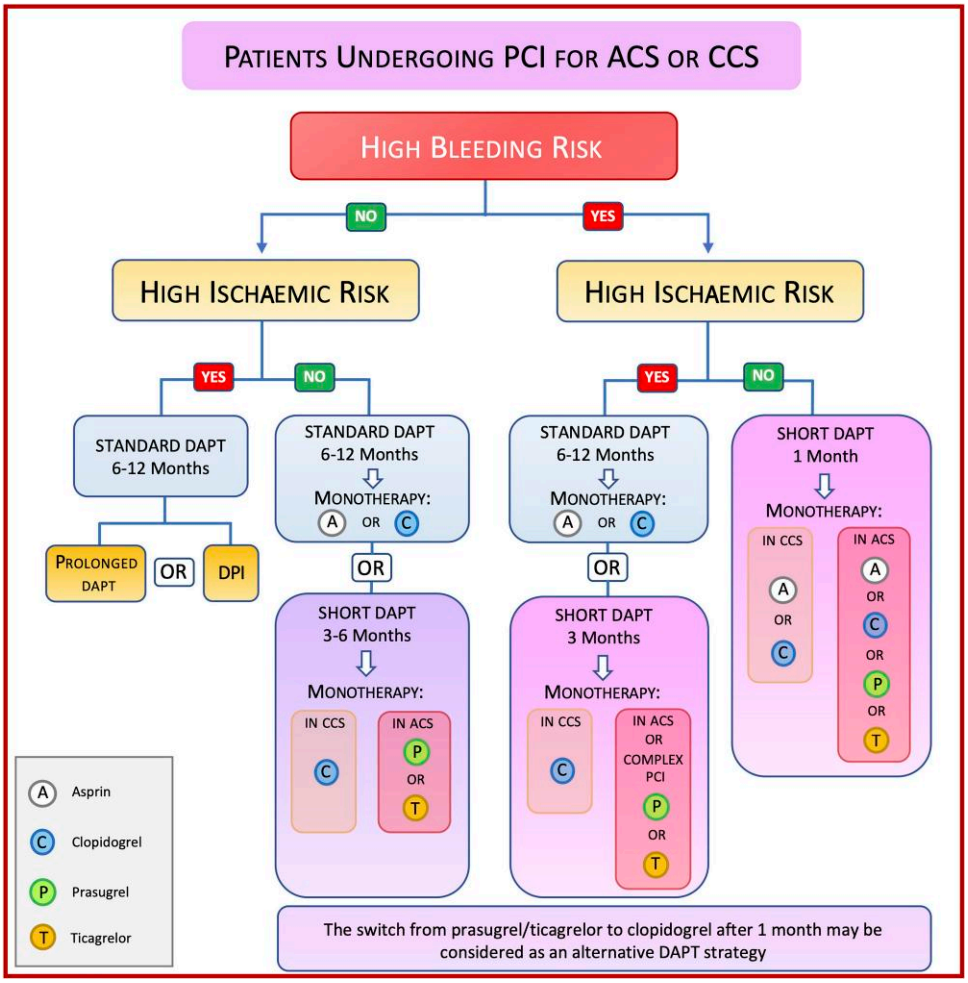

Figure 3 Possible algorithm for a personalized selection process of different antiplatelet strategies according to individual bleeding and ischaemic risk. A, aspirin; C, clopidogrel, ACS, acute coronary syndrome; CCS, chronic coronary syndrome; DAPT, dual antiplatelet therapy; DPI, dual pathway inhibition; PCI, percutaneous coronary intervention; P, prasugrel; T, ticagrelor

DAPT course vs. standard-duration DAPT in ACS populations, will provide more insights on the use of aspirin-free antiplatelet approaches following PCI.

Supplementary data

Supplementary data are not available at *European Heart Journal* online.

Declarations

Disclosure of Interest

P.C. declares speaker honoraria from Chiesi, Amgen, and Daiichi Sankyo. D.M. declares serving on the DSMB for Janssen Pharmaceuticals. D.C. declares speaker honoraria from Chiesi, Novo Nordisk, Sanofi, and Terumo.

Data Availability

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Table 4 Ongoing randomized trials on aspirin-free approaches after percutaneous coronary interventions in patients without concomitant indication to oral anticoagulation

Trial	*n* of patients	Population	Intervention	Control	Primary outcomes
Trials comparing the $P2Y_{12}$ inhibitor monotherapy after short DAPT (1 or 3 months) vs. standard DAPT in ACS patients undergoing PCI					
BULK-STEMI	$n = 1002$	Patients with STEMI undergoing PCI receiving DAPT with ticagrelor plus aspirin for 3 months	Ticagrelor (SAPT)	Ticagrelor plus aspirin (DAPT)	NACE at 12 months, MACCE at 12 months, and BARC type 3 or 5 bleeding at 12 months
COMPARE STEMI ONE	$n = 1608$	Patients with STEMI undergoing PCI receiving DAPT with prasugrel plus aspirin for 30–45 days	Prasugrel (SAPT)	Prasugrel plus aspirin (DAPT)	NACE at 11 months post randomization
ULTIMATE-DAPT	$n = 3486$	Patients with ACS undergoing PCI who are free from events at 1 month following DAPT with ticagrelor plus aspirin	Ticagrelor plus matching placebo (SAPT)	Ticagrelor plus aspirin (DAPT)	MACCE between 1 and 12 months and BARC type ≥2 bleeding between 1 and 12 months after PCI
TARGET FIRST	$n = 2246$	Patients with MI undergoing PCI, receiving DAPT with clopidogrel, prasugrel, or ticagrelor plus aspirin for 1 month	Clopidogrel, prasugrel, or ticagrelor (SAPT)	Clopidogrel, prasugrel, or ticagrelor plus aspirin (DAPT)	NACE between 1 and 12 months after PCI and BARC type ≥2 bleeding between 1 and 12 months after PCI
MATE	$n = 2856$	Patients with ACS undergoing PCI, receiving DAPT with ticagrelor plus aspirin for 1 month	Low-dose ticagrelor followed by clopidogrel (SAPT)	Ticagrelor plus aspirin (DAPT)	NACE at 12 months
Trials comparing the $P2Y_{12}$ inhibitor monotherapy after very short DAPT (mostly discontinued immediately after PCI) vs. standard DAPT					
NEOMINDSET	$n = 3400$	Patients with ACS undergoing PCI	Ticagrelor or prasugrel (SAPT)	Ticagrelor or prasugrel plus aspirin (DAPT)	MACCE at 12 months and BARC type ≥2 bleeding at 12 months
LEGACY	$n = 3090$	Patients with NSTE-ACS undergoing PCI	Clopidogrel, prasugrel, or ticagrelor (SAPT)	Clopidogrel, prasugrel, or ticagrelor plus aspirin (DAPT)	MACCE at 12 months and BARC type 2, 3, or 5 bleeding at 12 months
Trials comparing the $P2Y_{12}$ inhibitor monotherapy after DAPT discontinuation from 9 to 12 months after PCI vs. prolonged DAPT					
SMART-CHOICE 2	$n = 1520$	Patients undergoing PCI free from MACCE during DAPT for 12 months after PCI	Clopidogrel or low-dose ticagrelor (SAPT)	Clopidogrel or low-dose ticagrelor plus aspirin (DAPT)	MACCE at 24 months
Trials comparing the $P2Y_{12}$ inhibitor monotherapy vs. aspirin monotherapy after DAPT discontinuation					
SMART-CHOICE 3	$n = 5000$	Patients at 12 months after PCI discontinuing DAPT	Clopidogrel (SAPT)	Aspirin (SAPT)	MACCE at 12 months

ACS, acute coronary syndromes; BARC, Bleeding Academic Research Consortium; DAPT, dual antiplatelet therapy; MACCE, major adverse cardiac or cerebrovascular events; MI, myocardial infarction; NACCE, net adverse cardiac or cerebrovascular events; NACE, net adverse cardiac events; NSTE-ACS, non–ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; SAPT, single antiplatelet therapy.

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