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VIEWPOINT

Identifying the "Optimal" Duration of Dual Antiplatelet Therapy After Drug-Eluting Stent Revascularization

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Uncertainty regarding the appropriate duration of dual antiplatelet therapy (DAPT) with aspirin and a thienopyridine challenges every clinician involved in the care of patients considered for or treated with drug-eluting stents (DES). Despite guideline recommendations for extended (≥12 months) DAPT following percutaneous coronary revascularization with DES, few data are available to guide clinical decision-making beyond consensus opinion. Yet considering the clinical implications of stent thrombosis (ST) and its unpredictability in late occurring events, comprehensive assessment of the relationship between DAPT duration and ST over the long-term is a focus for DES-related clinical trials and an essential public health measure. Despite the potential for prolonged DAPT to reduce late-term cardiovascular events related to the progression of atherosclerosis, few studies have formally examined the safety and efficacy of extended DAPT and its impact on late ST events. The purpose of this paper is to appraise the existing evidence regarding the relationship between long-term DAPT and late cardiovascular events; address outstanding (and unstudied) dilemmas related to DAPT in DES-treated patients; and propose considerations for both trial design and clinical practice. (J Am Coll Cardiol Intv 2009;2:1279–85) © 2009 by the American College of Cardiology Foundation

An unresolved area of investigation in drug-eluting stent (DES) studies has been whether the risk of late (30 days to 1 year) and very late (beyond 1 year) stent thrombosis (ST) might be mitigated by the use of dual antiplatelet therapy (DAPT) (aspirin plus thienopyridine) beyond that described in early pre-approval trials that served as a basis for product labeling (1,2). Although a reanalysis of key randomized trials comparing sirolimus- and paclitaxel-eluting stents with bare-metal stents (BMS) through 5-year follow-up has demonstrated a numerically higher incidence of very late ST with DES (3–5), and observational studies have indicated a higher risk of ST in off-label indications for both BMS and DES (6,7), few data are available to guide clinical decision-making regarding long-term DAPT use.

Development of DAPT Guideline Recommendations: A Brief History

As a precautionary measure on the basis of trials associating "early" (≤6 months) thienopyridine discontinuation with risk of DES thrombosis, an

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inter-society guidelines recommendation advocated 12 months DAPT after DES placement in patients without contraindications and bleeding risk (8,9). In December 2006, after an extensive review of existing data indicating a numerical excess of late ST with sirolimus- and paclitaxel-eluting stents (3–5), the U.S. Food and Drug Administration advisory panel supported this empiric recommendation of 12 months DAPT after DES placement and determined that these guidelines be incorporated into DES product labeling. This recommendation was subsequently reinforced by a multidisciplinary Science Advisory statement for instructing clinical practice (2). Importantly, however, this recommendation was not based on any prospective randomized trial evidence associating extended-duration DAPT with a reduction in late ST; rather, the recommendation was based on consensus opinion derived from randomized trials evaluating thienopyridine dosing and treatment strategies involving BMS in clinical scenarios outside the approved indications for DES (10,11) and from observational studies indicating lower risk of death and myocardial infarction (MI) with long-term DAPT (12,13).

Abbreviations and Acronyms

BMS = bare-metal stent(s)
DAPT = dual antiplatelet therapy
DES = drug-eluting stent(s)
MI = myocardial infarction
PCI = percutaneous coronary intervention
ST = stent thrombosis

Long-Term DAPT After DES Revascularization: What Is the Evidence Basis?

Defining the potential benefit of long-term DAPT: prevention of target- versus nontarget lesion-related events. At present, studies examining the relationship between DAPT and outcomes after percutaneous coronary intervention (PCI) have been limited by trial design or methods that have restricted their applicability to clinical decision-making in routine practice. Given the focus on DAPT to reduce ST, discontinuation of antiplatelet therapy should be considered as "early," ≤6 months; "late," >6 and ≤12 months; and "very late," >12 months. Whereas observational studies have consistently established early discontinuation of DAPT with a higher risk of ST (14–17), additional studies have demonstrated that long-term DAPT might be associated with reductions in death and MI (12,13). However, long-term DAPT, although providing ischemic benefit, might not influence stent-specific events. In the Duke Cardiovascular Database, for example, patients treated with DES and a 2-year DAPT duration experienced significantly lower rates of death and MI compared with DES- and BMS-treated patients treated with shorter duration DAPT, although rates of ST were not reported (12). In addition, in a recent observational study of 749 diabetic patients who underwent percutaneous revascularization with either BMS or DES, a longer duration (i.e., >6 months) of clopidogrel use was associated with a lower incidence of death or MI over 2 years of follow-up, although the treatment effect did not differ according to stent type (13). For patients who discontinued clopidogrel <6 months in this study, the incidence of death or MI were similar, irrespective of treatment with BMS or DES. Thus, the benefit of long-term DAPT, especially in patients at high risk for recurrent ischemic events (e.g., acute coronary syndromes), might be related more to prevention of vascular thrombotic events due to progression of atherosclerosis rather than to the site of prior stent placement. In the only prospective, randomized trial to date, the CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance) trial demonstrated a significant reduction in late (median follow-up 27 months) ischemic events with long-term aspirin and clopidogrel compared with aspirin and placebo for patients with established vascular disease (18). Although a reduction in subsequent MI and stroke with prolonged DAPT was observed in patients with prior MI, stroke, or symptomatic peripheral arterial disease, no benefit was identified among those with established vascular disease but without a prior event.

Influence of DAPT on Late ST: Effect or Epiphenomenon?

Trials examining the relationship between DAPT discontinuation and ST. A common statistical misinterpretation is to associate 2 potentially independent observations (e.g., thienopyridine discontinuation and ST) as related or causative to one another. It is especially common to associate a relationship between a common event (e.g., thienopyridine discontinuation) and a rare event (e.g., late ST). This is particularly relevant to understanding the relationship between DAPT and late and very late ST, given that DAPT discontinuation is proportionate with time.

At present, observational studies specifically examining the relationship between DAPT duration and ST events have more commonly demonstrated that extended DAPT beyond 6 to 12 months is not associated with a reduction in late and very late ST (Table 1). In a prospective observational cohort study of 3,021 patients treated with DES and with follow-up through 18 months, the overall incidence of ST was 1.9% (19). Although the strongest predictor of ST was thienopyridine discontinuation within 6 months of stent placement, thienopyridine discontinuation after 6 months did not predict its occurrence. Recently, a single-center analysis identified 30-day and 6-month discontinuation but not cessation at 1 year (20) as predictors of ST. In a multicenter Korean registry of 7,221 patients undergoing PCI (43.8% DES), overall adjusted risks of death, death/MI, and target lesion revascularization were significantly lower with DES compared with BMS, even though DES

Table 1. Studies Examining the Relationship Between DAPT Duration and Late/Very Late ST After DES Revascularization

Authors (Ref. #)	Study Population, n	Study Duration	Death	MI	ST	Comments
Airoldi et al. (19)	3,021 DES	18 months	ST cases: 39%	ST cases: 79%	Overall rate 1.9%; HR for TP cessation: <6 months, 13.7 (CI: 4.0–46.7), >6 months, 0.94 (0.3–2.98)	Protective effect of TP on ST observed only within first 6 months of DES treatment; median time to ST from TP discontinuation: 14 days within first 6 months, 90 days thereafter
Park et al. (21)	2,873 DES patients 12-month event-free	3 yrs	HR: 1.20 (CI: 0.55–2.66) for continuing TP beyond 1 yr vs. discontinuation	HR: 0.53 (CI: 0.07–4.11) for continuing TP beyond 1 yr vs. discontinuation	HR: 0.54 (CI: 0.07–4.23) for continuing TP beyond 1 yr vs. discontinuation	No reduction in major adverse events with TP continuation beyond 1 yr in 12-month event-free patients; outcomes adjusting according to propensity score model
Schulz et al. (23)	6,816 DES	4 yrs	4.2% (overall)	8.6% (overall)	HR/day for ST at ≤6 months vs. >6 months: 0.98 (CI: 0.98–0.99) vs. 1.00 (CI: 0.99–1.01)	Protective effect of TP on ST observed only within first 6 months of DES treatment; median time interval from TP discontinuation to ST was 9 days within first 6 months vs. 104 days thereafter
Roy et al. (20)	2,889 DES	1 yr	N/A	N/A	Odds ratios for TP cessation: 30 days, 4.5 (CI: 2.0–10.4); 6 months, 2.4 (CI: 1.2–4.9); 1 yr, 1.7 (0.9–3.1)	Protective effect of TP on ST not observed past 6 months; TP compliance 73.8% in patients presenting with ST (82.6% for early ST, 43.8% for late ST)
Kimura et al. (22)	10,778 SES	2 yrs	On TP, 3.4%; off TP, 3.4%	On TP, 0.6%; off TP, 0.8%	No significant difference in definite ST at any time interval through 730 days between on and off TP	Adjusted event rates; discontinuation of both aspirin and TP associated with definite ST at any time point
van Werkum et al. (24)	21,009 DES and BMS	30.9 months	N/A	N/A	HR for TP cessation: <30 days, 36.5 (CI: 8.0–167.8); 180–365 days, 5.9 (CI: 1.7–19.8)	ST also associated with stent undersizing, TIMI flow grade <3, present malignancy, nontarget lesion target vessel disease, dissection, lack of aspirin, bifurcation, and young age

BMS = bare-metal stent(s); CI = confidence interval; DAPT = dual antiplatelet therapy; DES = drug-eluting stent(s); HR = hazard ratio; MI = myocardial infarction; N/A = not available; SES = sirolimus-eluting stent(s); ST = stent thrombosis; TIMI = Thrombolysis In Myocardial Infarction; TP = thienopyridine.

were associated with an increased risk of very late ST (21). However, among DES patients, continuing clopidogrel treatment beyond 12 months was not associated with a reduced risk for late-term ST, death, or the composite end point of death/MI, indicating that prolonged DAPT might not influence late thrombotic events. Similarly, in the largest of observational studies relating thienopyridine discontinuation with ST risk, the Japan Cypher Registry investigators reported outcomes related to thienopyridine adherence for 10,778 patients treated with sirolimus-eluting stents (22). Through 2-year follow-up, patients who discontinued both aspirin and thienopyridine treatment had significantly higher rates of ST compared with those patients who continued both medications. Thus, these results also underscore the importance of aspirin treatment. However, when discontinuation of both antiplatelet agents was considered, patients who discontinued thienopyridine but continued aspirin did not have an excess of ST at any time interval evaluated. Furthermore, 2-year rates of death or MI were identical (4.1%) in a 6-month landmark analysis comparing patients taking and not taking thienopyridine therapy. In the longest-term follow-up evaluating ST outcomes and thienopyridine treatment, a recent study from the ISAR (Intracoronary Stenting and Antithrombotic Regimen) group of 6,816 patients (4-year ST cumulative definite ST risk 1.2%) also showed no influence of continued thienopyridine treatment beyond the initial 6 months for reducing the risk of late and very late ST (23). These consistent findings are only countered to date by a case-controlled observational study from the Netherlands involving 21,009 patients for whom clopidogrel withdrawal within the initial 6 months was most predictive of ST events; most events during this time period occurred within 14 days of clopidogrel cessation, underscoring the dependency on the early and intermediate-term antithrombotic efficacy of DAPT (24). In this particular study, however, discontinuation of clopidogrel beyond 6 months was also significantly associated with a risk of ST, although the number of late ST events was low, and the strength of this relationship was considerably less than at earlier time points.

Balancing efficacy with bleeding risk. Few studies formally evaluated compliance with intended therapy and increased bleeding risks associated with long-term DAPT, and present guideline recommendations reflect uncertainty of

continuing DAPT beyond 1 year (Class IIb, Level of Evidence: C) (9). In the CHARISMA trial (18), among patients with established vascular disease, the rate of severe bleeding (fatal bleeding, intracranial hemorrhage, or bleeding that resulted in hemodynamic compromise or required blood transfusion and/or other medical intervention) was 1.7%, which exceeds most estimates of ST over a similar time interval (3–5,23). Although this same analysis indicated that bleeding events might decline beyond 9 months of DAPT, the potential to exclude patients who discontinued antiplatelet therapy for early bleeding events might represent an ascertainment bias and limit any definitive conclusion that prolonged DAPT is safe should bleeding not occur in the first year.

Can DAPT suppress all ST events regardless of cause? Finally, whether mechanisms of ST differ at variable time intervals after revascularization must be considered, in addition to the relative effect of antiplatelet therapy to reduce such risk. Within the early period after stent revascularization (i.e., 30 days), the underlying mechanism of ST might be related to mechanical factors including residual dissection or incomplete stent apposition and expansion. Stent thrombosis occurring over later periods might be related to delayed healing, impaired stent endothelialization, endothelial dysfunction, abnormal vessel wall remodeling, and/or polymer-mediated hypersensitivity that might persist beyond 1 year, if not indefinitely. In such instances of varied underlying pathology, whether DAPT might be sufficient to suppress thrombosis is hypothetical but unproven. Nevertheless, cases of late DES-related thrombosis might also occur despite continued DAPT (25,26). Among the 12 very late ST events in the recently reported 3-year follow-up of the ENDEAVOR IV (Randomized Comparison of Zotarolimus- and Paclitaxel-Eluting Stents in Patients With Coronary Artery Disease) trial, for example, 5 patients were taking DAPT at the time of the event, and 4 patients were receiving aspirin therapy alone (26).

Alternative thienopyridine agents. At present, no comparative studies examining dual antiplatelet treatment duration with aspirin and alternative thienopyridine agents (e.g., prasugrel, ticagrelor) after DES revascularization have been performed. However, recent comparisons of clopidogrel with prasugrel and ticagrelor among patients with acute coronary syndromes undergoing PCI have been the first to demonstrate differences in ST rates between thienopyridine agents (27,28). Among patients taking aspirin, ST at 15 months occurred in 2.4% of patients assigned to clopidogrel versus 1.1% among those randomized to prasugrel ($p < 0.001$). Although most ST events occurred within 30 days of initial revascularization, a benefit with prasugrel persisted beyond this timeframe through the entire study period. Overall, however, prasugrel therapy was associated with significantly greater bleeding risk, and potential reductions in ischemic events must be carefully considered relative to individual bleeding risk. Alternatively, definite ST through 12 months was significantly less common among patients treated with ticagrelor compared with clopidogrel (1.3% vs. 1.9%, $p = 0.009$) without a concomitant increased risk of major bleeding (28).

DAPT Permanent Discontinuation Versus Transient Interruption

A familiar limitation to population-based analyses related to DAPT duration is that few studies have precisely determined whether thienopyridine discontinuation is permanent or temporary. For instances of DAPT interruption, assessment of outcomes might be confounded if patients are considered off thienopyridine treatment at an earlier assessment but have instead later resumed therapy. Furthermore, reasons for DAPT discontinuation or transient interruption are also poorly understood. In the PREMIER (Prospective Registry Evaluating Myocardial Infarction: Events and Recovery) registry of patients treated with DES for acute MI, factors associated with thienopyridine noncompliance within the initial 30 days of revascularization included lower education level, advanced age, avoidance of health care because of cost, lack of discharge counseling, and history of pre-existing cardiovascular disease or anemia (29).

Timing of ST after DAPT discontinuation. A common clinical uncertainty related to DAPT interruption (aspirin, thienopyridine, or both drugs) is the relationship between time from DES revascularization, likelihood for ST and the temporal relationship between discontinuation and adverse event. When DAPT therapy is discontinued (or interrupted) within the initial 6 months of DES treatment, the time from drug cessation to ST is brief (19,24,30); beyond 6 months, however, the relationship between time from thienopyridine discontinuation and event is less distinct (19,24,30). As an example, in an overview of 161 ST cases pooled from 84 published reports, the median time to event was 10 days or less for patients who discontinued aspirin and thienopyridine therapy but 122 days for patients who stopped thienopyridine yet maintained acetylsalicylic acid (29). Only 6% of ST events occurred within 10 days in this latter group, suggesting the relative importance of maintaining aspirin treatment over thienopyridine for prevention of early events in circumstances requiring temporary antiplatelet discontinuation.

Safety of brief DAPT interruption and permanent discontinuation. Recently, 2 studies have taken different approaches toward prospectively evaluating outcomes related to intentional thienopyridine discontinuation versus unplanned interruption. In the SENS (Non-cardiac Surgical Procedures and Brief Interruption of Dual Antiplatelet Agents within 12 Months Following Endeavor Stent Implantation) trial (n = 3,099), outcomes were reported among 194 patients (6.3%)

who required noncardiac surgery and DAPT discontinuation within 1 year of coronary revascularization with zotarolimus-eluting stents (31). The most common reasons for brief interruption were related to dental, orthopedic, and endoscopic procedures. Thirty-day perioperative adverse events were identified in 4 patients (2.1%; 2 deaths, 2 MI). Three of the events occurred when surgery was performed within 3 months of DES revascularization, advocating delay of elective surgical procedures at least beyond this timeframe. Although the overall event rate is favorable for such high-risk patients, whether perioperative outcomes might be further improved with shorter-acting, reversible P_2Y_{12} platelet receptor antagonists (e.g., cangrelor, ticagrelor, or elinogrel) is uncertain.

In comparison, the multicenter DATE (Optimal Duration of Dual Antiplatelet Therapy After Implantation of the Endeavor Stent) trial recently examined 1-year outcomes among patients (n = 823) treated with zotarolimus-eluting stents for whom thienopyridine discontinuation was prespecified 3 months after PCI (32). High-risk anatomical and clinical complexities (e.g., unprotected left main, recent MI) were excluded. At 3 months, 81% (n = 666) of patients discontinued thienopyridine therapy per protocol. One-year rates of death, MI, and ST were 0.3%, 0.2%, and 0.2%, respectively. Conversely, adverse events, including repeat revascularization, were more common among patients continuing DAPT, although this observation might reflect a treatment bias. Although this study is also limited in design and sample size, as with the SENS trial, both studies indicate that either brief interruption or intentional cessation of thienopyridine treatment after zotarolimus-eluting stent revascularization might be associated with reasonable safety and encourage additional study (Table 2).

Identifying the "Optimal" DAPT Duration: Considerations for Clinical Trial Design and End Point Selection

At present, our understanding of the relationship between late antiplatelet therapy discontinuation and ST is based exclusively on studies that are limited by observational design and unmeasured confounders. As a result, despite guideline recommendations for extended DAPT with aspirin and a thienopyridine after percutaneous coronary revascularization with DES (8,9), few data are available to guide clinical decision-making beyond consensus opinion. Yet considering the clinical implications of ST and its unpredictability in late-occurring events, comprehensive assessment of ST over the long-term is a focus for DES-related clinical trial programs. As an example, the U.S. Food and Drug Administration has supported the need for well-conducted studies to address the optimal duration of DAPT after DES placement with standardized end point definitions that classify the occurrence of ST according to the level of evidence and timing of the event (33). Clinical studies must closely monitor patient compliance with the recommended DAPT duration and extended therapy; frequency, duration, and implications of DAPT interruption; need for deferral of invasive procedures because of need for continued DAPT; and the rate of bleeding complications associated with DAPT. In addition, investigator-initiated and industry-sponsored trials are in development or enrolling (Table 2) that are specifically intended to examine whether variable durations of DAPT after DES revascularization impact the outcomes of cardiovascular death, MI, stroke, and ST. Given that these studies are intended to examine low-frequency, late-occurring events, many will be challenged by the requirements for adequate sample size for

Table 2. Prospective Clinical Trials Evaluating Outcomes According to Varied DAPT Regimens

Trial Name	Inclusion Group, n	DAPT Duration	DES Type	Primary End Point	Key Secondary End Point(s)
DAPT	20,645 12-month event-free	12 vs. 30 months*	All DES (n = 15,245), BMS (n = 5,400)	1. Death/MI/stroke at 33 months 2. Definite/probable ST at 33 months	GUSTO bleeding
ISAR-SAFE	6,000 6-month event-free	6 vs. 12 months*	All DES	Death/MI/stroke/TIMI major bleed at 15 months	Individual component end points, ARC ST
REAL-LATE	2,000 12-month event-free	12 vs. 24 months*	All DES	2-yr cardiac death/MI	ARC ST, bleeding
ZEST-LATE	2,000 12-month event-free	12 vs. 24 months*	SES, PES, ZES	2-yr death/MI	ARC ST, bleeding
OPTIMIZE	3,120 non-STEMI	3 vs. 12 months*	ZES	1-yr death/MI/stroke/TIMI major bleed	ARC ST
SEASIDE	900 non-ACS	6 months	ZES	1-yr death/MI/stroke	GUSTO bleeding
DATE	823 non-ACS	3 months	ZES	1-yr cardiac death/MI/ST	Individual component end points

All trials currently enrolling or completed (DATE trial). *Randomized trial design.

ACS = acute coronary syndrome; ARC = Academic Research Consortium; DATE = Optimal Duration of Dual Antiplatelet Therapy After Implantation of the Endeavor Stent; GUSTO = Global Use of Strategies to Open Occluded Coronary Arteries; ISAR-SAFE = Intracoronary Stenting and Antithrombotic Regimen: Safety And EFficacy of Six Months Dual Antiplatelet Therapy After Drug-Eluting Stenting; PES = paclitaxel-eluting stent(s); REAL-LATE = Correlation of Clopidogrel Therapy Discontinuation in REAL-world Patients Treated with Drug-Eluting Stent Implantation and Late Coronary Arterial Thrombotic Events; SEASIDE = Scripps Evaluation of Antiplatelet Therapies for Intermediate Duration With the Endeavor Stent(s); SENS = Non-cardiac Surgical Procedures and Brief Interruption of Dual Antiplatelet Agents within 12 Months Following Endeavor Stent Implantation; ZES = zotarolimus-eluting stent(s); ZEST-LATE = Evaluation of the Long-Term Safety After Zotarolimus-Eluting Stent, Sirolimus-Eluting Stent, or PacliTaxel-Eluting Stent Implantation for Coronary Lesions–Late Coronary Arterial Thrombotic Events; other abbreviations as in Table 1.

statistical power and dedicated long-term follow-up. Furthermore, noting the 1) variable durations of DAPT being evaluated in these trials; 2) potential differences in ST between thienopyridine agents (27,28) and possibly DES (34,35); 3) interindividual variability in antiplatelet therapy response (36); and 4) differences in enrollment criteria (inclusion of event-free patients vs. all-comers, all DES vs. specific DES), it is likely that the impact of any singular trial on clinical decision-making will be varied, and trial results must be weighed against their design and methods.

The dilemma for practitioners and suggestions for clinical practice. In light of the limitations identified with the guidelines recommendation, current evidence raises more questions and leaves several outstanding issues unaddressed in clinical practice. Especially, more detailed clinical trials information is needed to refine the existing 12-month DAPT recommendations, yet identifying the "optimal" duration of DAPT for an all-comer PCI population seems an oversimplification. Is the "optimal" duration of DAPT the same for all DES, recognizing potential differences in safety outcomes of cardiac death, MI, and ST? Similarly, understanding the potential for inherited variation in platelet responsiveness and its contribution to ST (36), is there a role for genomic- and platelet assay-based tailored therapy (37)? What are the consequences of brief interruption of DAPT for unplanned invasive procedures (e.g., noncardiac surgery)? Is the potential benefit of long-term DAPT outweighed by a higher risk of major bleeding? Will measurable differences exist between clopidogrel and newer, direct P_2Y_{12} inhibitors (e.g., prasugrel, ticagrelor) with prolonged therapy after PCI in real-world settings? These outstanding issues have important implications for both clinical research and routine clinical decision-making.

The dilemma for clinicians is not simply whether it is safe to discontinue thienopyridine treatment after DES revascularization before 12 months but instead whether continuing long-term DAPT is both effective and safe. We believe the rationale for a lifetime commitment to DAPT uniformly in patients undergoing DES revascularization is unsubstantiated: bleeding and economic costs of prolonged treatment might outweigh any potential reduction in stent thrombotic events, and if patients are treated with long-term (>12 months) DAPT, clinicians must recognize they are likely treating systemic disease rather than the stent territory. Thus, long-term DAPT might have real potential benefit, especially in patients with acute coronary syndromes or prior thrombotic events, but the rationale should not be driven by a reduction in late or very late ST, which remains as yet unproven. Nonetheless, until conclusive evidence is available to revise the current recommendations for DAPT after DES revascularization, we consider 12 months of DAPT reasonable for most patients. However, a rationale exists to reconsider DAPT prescription for individuals on the basis of clinical presentation and risk assessment. For example, our practice pattern is to treat patients with acute or prior vascular events with even longer thienopyridine therapy (≥12 months) to prevent cardiovascular death, recurrent MI or stroke, provided they do not have significant bleeding risk (18,27). For patients with ST, we attempt to identify the underlying cause on the basis of clinical, angiographic, and intravascular ultrasound findings; measure residual platelet reactivity after clopidogrel; and consider treatment with prasugrel in the absence of contraindications. Alternatively, several current observational studies indicate that shorter DAPT duration (e.g., <12 months) might be sufficient to reduce ST risk compared with extended therapy. We believe this may particularly apply to patients with low clinical risk (e.g., patients without acute coronary syndromes or chronic kidney disease) and simple lesion complexity, in whom the antirestenotic benefit of DES is important. Such clinical decision-making must be individualized, and the decision to use DES in patients treated with DAPT durations shorter than 12 months must also take into consideration the reason(s) for abbreviated thienopyridine therapy (e.g., need for elective but foreseeable surgery, concurrent warfarin therapy), the relative benefit of DES over BMS, and in our opinion, the type of DES. We welcome evidence that will advance our understanding of an issue that challenges every clinician involved in the care of patients considered for or treated with DES.

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