Coronary artery disease (CAD) remains a principal source of morbidity and mortality among adults in both the developed world and the developing world. Despite important advances in medical therapy for CAD, revascularization is frequently necessary. Currently, nearly 2 million percutaneous coronary interventions (PCIs) are performed in the United States and Europe, and >90% of them entail the deployment of at least 1 coronary stent. The introduction of metallic coronary stents (bare metal stents [BMS]) 2 decades ago resulted in a significant reduction in the immediate and long-term complications of PCI, particularly dissections, abrupt vessel closure, and need for repeat target lesion or target vessel revascularization. Abrupt vessel closure was essentially eliminated by stents. The incidence of target lesion and target vessel revascularization was halved from ≈20% to 25% at 1 year to 10% to 15%. Stents became further refined a decade ago by the addition of eluting antiproliferative agents embedded in durable or resorbable biopolymers (drug-eluting stents [DES]). This innovation further reduced the need for target vessel or target lesion revascularization to the single-digit range. 

Response by Becker and Helmy on p 2009

The persisting weaknesses of coronary stents, the propensity to provoke stent thrombosis (ST) and late neatherosclerosis, were not modified by the introduction of DES. In fact, a sentinel report in 2004 indicated that first-generation DES are prone to late (1–12 months) and very late (>12 months) ST because of their inherent delayed endothelialization. Intensive research into the causes and predictors of this phenomenon resulted in the current recommendations of the various professional societies to treat patients after DES implantation with 6 to 12 months of dual antiplatelet therapy (DAPT) consisting of aspirin and an ADP (P2Y12) receptor antagonist. This article reviews the evidence supporting the continuation of DAPT for ≥12 months and direct our attention to 2 important concepts:

1. Is DAPT meant to prevent device-oriented cardiac events or patient-oriented events? The latter refers to the classic end points of clinical trials such as any death, any myocardial infarction (MI), stroke, or any revascularization, whereas the former addresses stent-specific events such as ST, target vessel MI, or target lesion revascularization, with some obvious overlap between them.

2. Can prolonged DAPT prevent the formation of new or the progression of existing atherosclerotic lesions in segments remote from the target lesion?

Moreover, we need to address the dilemma facing the clinician with respect to whether all patients are treated in a similar fashion or whether tailoring of therapy is indicated according to existing comorbidity (diabetes mellitus, chronic kidney disease, etc), the burden of coronary disease, and the circumstances leading to PCI (elective setting versus acute coronary syndrome [ACS]).

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However, before we explore the data pertinent to this topic, it may be appropriate to review the current professional guidelines for DAPT after PCI with stenting.

**Recommendations for DAPT After PCI With DES**

The American professional societies (American College of Cardiology, American Heart Association, and Society for Coronary Angiography and Intervention) guidelines for PCI recommend DAPT for at least 12 months after PCI for ACS but allow a shorter duration if ACS is not present (Class I; Level of Evidence B) or the risk of bleeding is high regardless of context of PCI (Class IIa; Level of Evidence C). Continuation of DAPT beyond 12 months may be considered (Class IIb; Level of Evidence C).

The European Society of Cardiology, in its most recent guidelines for the management of and revascularization in patients with stable CAD, recommends DAPT for 6 months after PCI (Class I; Level of Evidence B) and allows even shorter duration if the risk of bleeding is high (Class IIb; Level of Evidence A) or a longer duration if the bleeding risk is low and ischemic risk is high (Class IIb; Level of Evidence C). In contrast, for patients with ACS or ST-segment–elevation MI, the European Society of Cardiology recommends 12 months of DAPT, regardless of revascularization status or stent used (Class I; Level of Evidence A).

In summary, American and European professional societies agree on the recommendation of (at least) 1 year of DAPT after PCI for ACS but differ on the recommendation for duration of DAPT after elective PCI. Remarkably, the initial trials with DES recommended DAPT for 2 to 3 months with sirolimus-eluting stents (eg, RAVEL) and 6 months with paclitaxel-eluting stents (eg, TAXUS II).

**Experimental Evidence Supporting Antiatherosclerotic Effect of DAPT**

Just as aspirin alone has been shown to reduce the rate of clinical events in patients with vascular disease of various presentations and after different interventions, the addition of platelet P2Y₁₂ ADP receptor antagonists was expected to contribute to further improvement in outcomes via important anti-inflammatory and antiatherosclerotic effects, beyond the inhibition of platelet function.

Azar et al randomized 73 patients with stable CAD to clopidogrel or placebo in addition to background aspirin therapy. Serum CD40 ligand decreased significantly at 8 weeks (P=0.03) in the clopidogrel group only. Serum CD40 ligand, an important mediator of inflammation, facilitates the deposition of atheroma in injured vascular endothelium (Figure 1). A few experimental studies in animals with induced atherosclerosis support this concept. Compared with placebo, clopidogrel reduced plaque size and increased its stability via a larger fibrous component, which is not prone to rupture. Clopidogrel also increased the number of atheroprotective regulatory CD4⁺CD25⁺ T cells. Similar reductions in neointima formation were observed in rabbits exposed to an atherosclerotic diet and treated with clopidogrel or placebo. Une et al reported that DAPT for 1 year after surgical revascularization reduced the progression of existing lesions compared with aspirin alone (P<0.01) and decreased the proportion of new occlusions (P=0.02).

The relationship between platelet inhibition and inflammation is complex, particularly because the connection between higher levels of inflammatory markers and atherosclerotic events may not be necessarily causative. DAPT inhibits the immediate inflammatory response after PCI, as shown in a large cohort of patients undergoing PCI. Clopidogrel pretreatment decreased the C-reactive protein surge after stenting by 65% and was an independent predictor of C-reactive protein level after adjustment for confounders. Lowering C-reactive protein levels may confer a long-term advantage, as evidenced by lower rates of events in patients with less vascular inflammation.

**Observational Data for Shorter Versus Longer Duration of DAPT After DES**

As is frequently the case, observations from registries hinted at a possible benefit of prolonged DAPT and spurred the execution of randomized, clinical trials.

Eisenstein et al evaluated the outcomes of 4666 patients stented with BMS (n=3165) or first-generation DES (n=1501) between 2000 and 2005. Among patients with DES who were free of events at 6 months, continued DAPT was a significant independent predictor of lower death (2.0% versus 5.3%; P=0.03) and lower death or MI (3.1% versus 7.2%; P=0.02) rates at 24 months compared with those on aspirin alone.

In an analysis from the Veterans Administration registry, among 1445 patients treated with PCI (34% DES) in 2003 to 2004 and followed up for 2 years, those on continued DAPT had significantly lower mortality than those off DAPT. Overall, in patients free of events at 6 months, cessation of DAPT was associated with a higher adjusted risk of death after DES (hazard ratio [HR]=3.57; 95% confidence interval [CI], 1.13–11.3; P=0.01).

Preliminary data from the Convergent Registry of Catholic and Chonnam University for Acute MI (COREA-AMI)
registry suggested that, after PCI for ST-segment-elevation MI in 2293 patients free of major adverse cardiac events or bleeding at 1 year, longer DAPT was associated with a lower rate of major adverse cardiac events (18.0% for 12–18 months, 10.2% for 18–24 months, and 8.9% for >24 months; \( P<0.001 \)).

Brar et al\(^{25} \) identified 749 patients with diabetes mellitus who underwent PCI with DES (n=491) or BMS (n=251) between 2002 and 2004. Among the 671 patients free of events after 6 months of DAPT, the incidence of death or MI was 3.2%, 9.4%, and 16.5% among those treated with DAPT for >9, 6 to 9, and <6 months, respectively (\( P<0.001 \)). Continued DAPT was an independent predictor of lower rates of death or MI for both DES (HR=0.22; 95% CI, 0.08–0.62; \( P=0.005 \)) and BMS (HR=0.25; 95% CI, 0.08–0.81; \( P=0.02 \)).

The Bern-Rotterdam registry of patients treated with DES analyzed the use of DAPT among patients with very late ST. Among 69 patients with this event between 1 and 4 years after PCI, only 20% were on DAPT, whereas 80% were not (\( P<0.05 \)).\(^{26} \) This observation is particularly important because it appears that implantation of a first-generation DES was associated with a constantly accumulating annual rate of definite ST of 0.4% to 0.6%.

The largest observational report comes from the Swedish Heart Registry (SWEDHEART).\(^{27} \) Patients with ACS were categorized according to duration of DAPT, and only those free of events at 3 months were included. Among 28,680 patients, 15,009 received DAPT for >3 months, and 6,640 were treated for >6 months. One third of the patients were not revascularized at all. The rate of death, re-MI, or stroke was 65.2 per 1000 person-years for ≤3 months or DAPT, 29.4 per 1000 person-years for 6 months of DAPT, and 20.4 per 1000 person-years for >6 months (\( P<0.0001 \)). This reduction in ischemic events was accompanied, as expected, by a higher rate of bleeding (adjusted HR=1.45; 95% CI, 1.14–1.86; \( P=0.003 \)).

The data mentioned above need to be interpreted with caution. Besides the fact that they do not reflect randomization to longer or shorter DAPT, it is very difficult to tease the reasons for continued DAPT in registries beyond a certain period. Common causes are recurrent events during the initial DAPT period necessitating its continuation or the desire to suppress atherosclerosis progression. In contrast, reasons for discontinuation may be financial difficulties, bleeding, or lack of evidence that more prolonged therapy affects outcomes favorably.

### Table. Randomized Trials of Longer Versus Shorter Duration of DAPT After Coronary Stenting

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year Published</th>
<th>n</th>
<th>Stable Angina/ Silent Ischemia, %</th>
<th>DAPT Duration, mo</th>
<th>Protocol Type*</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXCELLENT</td>
<td>2012</td>
<td>1443</td>
<td>48.4</td>
<td>6 vs 12</td>
<td>1</td>
</tr>
<tr>
<td>RESET</td>
<td>2012</td>
<td>2117</td>
<td>45.4</td>
<td>3 vs 12</td>
<td>1</td>
</tr>
<tr>
<td>PRODIGY</td>
<td>2012</td>
<td>1970</td>
<td>25.5</td>
<td>6 vs 24</td>
<td>2</td>
</tr>
<tr>
<td>OPTIMIZE</td>
<td>2013</td>
<td>3119</td>
<td>68.0</td>
<td>3 vs 12</td>
<td>1</td>
</tr>
<tr>
<td>SECURITY</td>
<td>2014</td>
<td>1399</td>
<td>61.6</td>
<td>6 vs 12</td>
<td>1</td>
</tr>
<tr>
<td>ISAR SAFE</td>
<td>2014</td>
<td>4005</td>
<td>59.8</td>
<td>6 vs 24</td>
<td>2</td>
</tr>
<tr>
<td>ITALIC</td>
<td>2014</td>
<td>1850</td>
<td>61.5</td>
<td>6 vs 24</td>
<td>2</td>
</tr>
<tr>
<td>REAL/ZESET LATE</td>
<td>2010</td>
<td>2701</td>
<td>37.6</td>
<td>12 vs 24</td>
<td>2</td>
</tr>
<tr>
<td>DAPT Study</td>
<td>2014</td>
<td>9961</td>
<td>73.9</td>
<td>12 vs 30</td>
<td>2</td>
</tr>
</tbody>
</table>

DAPT indicates Dual Anti-Platelet Therapy; EXCELLENT, Efficacy of XIence/Promus Versus Cypher to Reduce Late Loss in Stent; ISAR SAFE, Safety and Efficacy of Six Months Dual Antiplatelet Therapy After Drug-Eluting Stenting; ITALIC, Is There a Life for DES After Discontinuation of Clopidogrel; OPTIMIZE, Optimized Duration of Clopidogrel Therapy Following Treatment With the Endeavor Zotarolimus-Eluting Stent in the Real World Clinical Practice; PRODIGY, Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia; REAL, Correlation of Clopidogrel Therapy Discontinuation in Real-World Patients Treated With Drug-Eluting Stent Implantation; RESET, Real Safety and Efficacy of 3-Month Dual Antiplatelet Therapy Following Endeavor Zotarolimus-Eluting Stent Implantation; SECURITY, Second Generation Drug-Eluting Stents Implantation Followed by Six Versus Twelve-Month Dual Antiplatelet Therapy; and 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 Artery Thrombotic Events. The first 7 trials compared <12 months of DAPT with at least 12 months of DAPT. The last 2 trials compared 12 months of DAPT with longer durations (in order of publication). EDUCATE data were already included in DAPT.

*1 indicates trials with enrollment after percutaneous coronary intervention; and, 2, trials with enrollment after patients had been free of events for a prespecified period of DAPT.

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**Randomized Comparison of Shorter Versus Longer Duration of DAPT After DES**

Nine randomized, clinical trials evaluated at least 12 months versus a shorter duration of DAPT in patients undergoing PCI with DES. The majority compared exactly 12 months of DAPT with a shorter duration of therapy (Table and Figure 2).

The Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss in Stent (EXCELLENT) trial randomized patients to 1 of the 2 stents (3:1) and to short- or long-duration DAPT (1:1). For the DAPT analysis, the primary end point of target vessel failure at 1 year (a composite of cardiac death, MI, or ischemia-driven target vessel revascularization) occurred in 4.8% and 4.3%, respectively (\( P=0.60 \)). It is notable that ST occurred in 0.9% and 0.1%, respectively (\( P=0.10 \)). In the pre-specified high-risk group of diabetic patients, target vessel failure was significantly more common in the short-duration DAPT group (HR=3.16; \( P=0.005 \)).

The Real Safety and Efficacy of 3-Month Dual Antiplatelet Therapy Following Endeavor Zotarolimus-Eluting Stent Implantation (RESET) trial tested very short-duration DAPT duration versus the conventional 12 months of DAPT after PCI with DES.\(^{29} \) There was no significant difference in the composite end point of cardiovascular death, MI, ST (definite or probable), ischemia-driven target vessel revascularization, or bleeding (Thrombolysis in Myocardial Infarction major or minor)\(^{31} \) at 1 year between the short- and long-duration DAPT regimens (4.7% versus 4.7%; \( P=0.84 \)). There was no ST in the short-duration DAPT group after 3 months.
The Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia Study (PRODIGY) compared 6 months of DAPT with 24 months of DAPT in patients receiving BMS or DES (first and second generations) who were free of adverse cardiac events at 30 days after the procedure.32 There was no difference in the primary end point of cardiovascular death, MI, or stroke at 2 years (10.0% versus 10.1%, respectively; *P* = 0.91). There was more bleeding (Bleeding Academic Research Consortium types II, III, and V)33 in the prolonged DAPT group (7.4% versus 3.5%, respectively; *P* = 0.0002). In a separate landmark analysis from this trial, patients assigned to first-generation DES (paclitaxel-eluting stents) had significantly higher rates of definite or probable ST when receiving only 6 months of DAPT.34 The inhibition of neointimal formation did not differ between the DAPT duration groups. In a subsequent analysis, patients undergoing treatment for in-stent restenosis (n=224) benefited from longer DAPT. The primary end point occurred in 16.7% of the short-duration DAPT group and 7.3% of the long-duration DAPT group (P=0.034), related predominantly to a higher rate of death or MI (15.5% versus 6.5%, respectively; P=0.03).35

The Second Generation Drug-Eluting Stents Implantation Followed by Six Versus Twelve-Month Dual Antiplatelet Therapy (SECURITY) trial randomized patients stented with second-generation DES to short- or long-duration DAPT. At 1 year, a third of the patients in the 6-month DAPT group were still on DAPT. The primary end point of cardiac death, MI, stroke, definite or probable ST, and Bleeding Academic Research Consortium bleeding types III or IV at 12 months occurred in 4.5% versus 3.7%, respectively (P=0.47), confirming noninferiority of the 2 regimens (P<0.05). Prolonged DAPT beyond 6 months was not an independent predictor of the primary end point at 12 months (HR=1.27; 95% CI, 0.75–2.15; *P*=0.37).

The Safety and Efficacy of Six Months Dual Antiplatelet Therapy After Drug-Eluting Stenting (ISAR-SAFE), presented at the 2014 American Heart Association Annual Scientific Meeting, also tested short- versus long-duration DAPT in patients who were free of events at 6 months after PCI.36 The trial was discontinued prematurely as a result of low enrollment and lower-than-expected event rates. The composite end point of death, MI, stroke, or ST was not different between the 2 groups at 9 months after randomization (1.3% versus 1.5%; *P*=0.57).
on-therapy results at 1 year after randomization. The trial was discontinued prematurely because of low enrollment and lower-than-expected event rates. The primary end point (cardiovascular death, MI, stroke, emergency revascularization, or thrombolysis in myocardial infarction major bleeding) was not different between the groups (1.5% versus 1.6%, respectively; \( P=0.85 \)).

A combination of 2 randomized, clinical trials, the Correlation of Clopidogrel Therapy Discontinuation in Real-World Patients Treated With Drug-Eluting Stent Implantation and Late Coronary Arterial Thrombotic Events (REAL-LATE) and the 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 (ZEST-LATE), which had similar study designs, evaluated patients free of major adverse cardiac events after 12 months of DAPT after DES implantation who were assigned to monotherapy or to DAPT for another 12 months. The 2 trials could not be completed because of low enrollment and were not reported separately. There were no significant differences in the rates of cardiac death or MI (1.2% versus 1.8%, respectively; \( P=0.17 \)) or of ST (0.4% in both groups; \( P=0.76 \)) between the groups. The incidence of death, MI, or stroke, however, was higher in the extended DAPT group compared with the aspirin alone group (3.2% versus 1.8%; \( P=0.05 \)). Bleeding rates were very low and comparable in the 2 groups.

The DAPT Study comparing 12 and 30 months of DAPT (65% clopidogrel, 35% prasugrel) in nearly 10,000 patients without clinical events 1 year after PCI showed a significant reduction in the composite of death, MI, or stroke among the longer-duration DAPT group (4.3% versus 5.9%; HR=0.71; 95% CI, 0.59–0.85; \( P<0.001 \)), driven predominantly by a reduction in MI. There also was a robust reduction in the incidence of definite or probable ST (0.4% versus 1.4%, respectively; \( P<0.001 \)) and, importantly, a reduction in non-stent-related MI (1.8% versus 2.9%, respectively; \( P<0.001 \); Figure 3). In contrast the incidence of moderate or severe bleeding (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries [GUSTO] scale) was higher in the extended DAPT group (2.5% versus 1.6%; \( P=0.001 \)), negating much of the reduction in ischemic events. It is notable that overall death rates were higher in the prolonged DAPT group at 33 months (2.3% versus 1.8%; HR=1.36; 95% CI, 1.02–1.82; \( P=0.04 \)). This excess was exclusively the result of a higher rate of noncardiovascular death (1.0% versus 0.5%; \( P=0.002 \)), presumably related to a higher rate of pre-existing cancer in the prolonged DAPT group. Nevertheless, more noncardiovascular death related to bleeding occurred in the extended DAPT group. The US Federal Drug Administration is currently reviewing the individual patient data for more details. The benefit of extended DAPT was more pronounced in men and in nondiabetics.

It is important to realize that the designs of these 9 trials differ significantly in the fact that some included patients only after having been free of events at the end of a period of DAPT (PRODIGY, REAL, ISAR SAFE, ITALIC, and DAPT), whereas others (EXCELLENT, OPTIMIZE, RESET, and SECURITY) randomized patients immediately after PCI, thus having potentially a higher rate of events. Most of them (DAPT is the notable exception) were designed as noninferiority trials, thus not excluding the possibility that a small benefit may exist for longer DAPT, particularly for very rare events such as ST. The follow-up period was also quite short in the trials with a noninferiority design, precluding the opportunity to observe reduction in events not related to stents, essentially secondary prevention of CAD progression. EXCELLENT, REAL, and DAPT did not include bleeding in their primary end point.

The most innovative approach is tested currently in the GLOBAL LEADERS: A Clinical Study Comparing Two

![Figure 3. Incidence of non-stent-related myocardial infarction (MI) in the Dual Antiplatelet Therapy trial. HR indicates hazard ratio. Adapted from Mauri et al with permission from the publisher. Copyright © 2014 Massachusetts Medical Society. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.](image-url)
Forms of Anti-platelet Therapy After Stent Implantation (http://www.clinicaltrials.gov; NCT01813435), in which ≈20000 patients were randomized to 12-month DAPT after PCI for ACS or to 1 month of aspirin and ticagrelor followed by 23 months of ticagrelor monotherapy. Results are expected by 2016.

Separating Device-Oriented Events From Patient-Oriented Events

Many of the guideline recommendations mentioned above either were based on consensus of opinion among experts or were shaped by the design of the existing randomized, clinical trials. For example, patients with ACS were treated for 9 to 15 months in 3 large trials of DAPT in ACS because these studies were event driven and it took this long to accumulate the number of events projected for sufficient statistical power.41-44 Shorter durations of therapy were not considered, and longer durations were not evaluated. It is evident from the rate of accumulation of events in these 3 trials that at least one quarter of all events occurred beyond the first 6 months, supporting the recommendations for prolonged DAPT in patients with ACS. Indeed, the only published randomized, clinical trials to date evaluating the benefit of prolonged DAPT (albeit compared with monotherapy, not compared with shorter DAPT duration) in patients with vascular disease also lend credence to this concept.45 The Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance (CHARISMA) study enrolled 15603 patients either with documented vascular disease (prior MI, prior stroke, multivessel revascularization, or symptomatic peripheral arterial disease) or at high risk for developing it. The entire cohort had a reduction with DAPT in the key secondary end point of cardiovascular death, MI, stroke, or rehospitalization for ACS, revascularization, or transient ischemic attack from 17.9% to 16.7% (P=0.04). Among the ≈80% of the patients enrolled for secondary prevention, DAPT for 30 months significantly reduced the rate of recurrent events compared with aspirin monotherapy (6.9% versus 7.9%, respectively; P=0.046; Figure 4). These results are somewhat echoed by the Clopidogrel for the Reduction of Events During Observation (CREDO) trial in which DAPT for 1 year was better at preventing death, MI, or stroke than aspirin alone after BMS (8.5% versus 11.7%, respectively; P=0.02).46

Importantly, accruing evidence appears to suggest that second-generation DES, particularly the cobalt-chromium everolimus-eluting stent, have nearly eliminated the continuing risk of very late ST observed with first-generation DES. In a network meta-analysis of 49 trials and 50 844 patients comparing various types of stents, the everolimus-eluting stent was associated with lower rates of definite ST compared with BMS (odds ratio, 0.35; 95% CI, 0.17–0.69; P<0.05) or paclitaxel-eluting stents (odds ratio, 0.34; 95% CI, 0.19–0.62; P<0.05) at 2 years.47-48 These data may imply that, because the rate of very late ST is reduced by the newer stents, the need for prolonged DAPT may also be lower, at least with respect to stent-oriented clinical events. Nevertheless, a prespecified analysis by stent type in the DAPT trial indicates that the benefit of longer DAPT is independent of stent type (first- versus second-generation DES; Pint=0.76).

Summary and Personal Interpretation

The current professional guideline recommendations for DAPT after PCI with DES are based on important data accrued from randomized, clinical trials that were not specifically designed to address the question of its duration. Observational data sets and experimental models indicate that longer and more effective DAPT may reduce ischemic events in patients treated with DES, particularly when high-risk characteristics such as large burden of atherosclerosis, recent ACS, diabetes mellitus, or restenosis are present. Almost invariably, longer exposure to DAPT leads to more bleeding, and the precise risk-to-benefit ratio for each patient can hardly be codified in an all-encompassing recommendation.

From my perspective, prolonged DAPT has a role in reducing patient-oriented adverse events (secondary prevention) and very late ST and its consequences after stent implantation, particularly in patients at high risk for recurrent ischemic events. I recommend it for as long as it is well tolerated and does not interfere with the application of other medical therapies.

Disclosures

Dr Brener serves as a consultant and speaker for AstraZeneca Ltd.

References


Response to Brener

Richard C. Becker, MD; Tarek Helmy, MD

Dr Brener presents a thoughtful perspective that at least 12 months of dual antiplatelet therapy is needed for all patients with drug-eluting stents. This overall premise considers: 1) the device, second generation drug-eluting stents with more favorable stent design, local drug concentration, transport kinetics, tissue binding properties in the vessel wall, and less flow separation, and 2) the patient, acknowledging that a 6-month treatment duration may be acceptable in (a) the absence of acute coronary syndrome as the indication for drug-eluting stents implantation and (b) high bleeding risk. The ability of dual antiplatelet therapy to impact the natural history of coronary arterial atherosclerosis is less compelling; yet, if the primary foundation for the hypothesis is based on platelet, vascular smooth muscle, and leukocyte and macrophage P2Y12 receptors, then monotherapy with a potent P2Y12 receptor antagonist, as supported in the Clopidogrel for the Reduction of Events During Observation (CREDO)-Kyoto Registry should become the next frontier of investigation. If the goal is to reduce the burden of atherosclerosis and its phenotypic expressions of disease, including myocardial infarction, ischemic stroke and cardiovascular death, then optimal medical therapy in patients with known coronary artery disease must surpass the 40% mark recently documented in the SYNTAX study. In the end, less may be more, and more may be gained by following the current guidelines masterfully crafted by the American College of Cardiology, American Heart Association, and European Society of Cardiology than by prescribing dual antiplatelet therapy indefinitely among patients undergoing stent implantation.
Are at Least 12 Months of Dual Antiplatelet Therapy Needed for All Patients With Drug-Eluting Stents? : All Patients With Drug-Eluting Stents Need at Least 12 Months of Dual Antiplatelet Therapy
Sorin J. Brener

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