Clinical update

Oral dual antiplatelet therapy: what have we learnt from recent trials?

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International guidelines recommend the use of aspirin treatment immediately and indefinitely in coronary patients. The optimal time to start and the duration of dual antiplatelet therapy (DAPT; aspirin plus a P2Y12 inhibitor) have not been clearly established. Recent clinical trials have provided important new information allowing for evidence-based decisions regarding timing of initiation and duration of DAPT. The benefit-to-risk ratio of DAPT pre-treatment appears to depend on the type of acute coronary syndrome, the time until angiography, and the onset of action of the drug. In stable patients undergoing percutaneous coronary intervention with the latest generation drug-eluting stents, patients should be treated for at least \(\approx 6\) months. Shorter courses of therapy may be necessary when special conditions occur (e.g. surgery; oral anticoagulation). Longer courses of therapy may be reasonable in patients at low bleeding risk who are tolerating DAPT well. For patients with ACS, prolonged DAPT is beneficial and therefore reasonable as long as the patient is tolerating the therapy. Individualized management of DAPT must be seen as a dynamic prescription with regular re-evaluations of the risk–benefit to the patient according to changes in his/her clinical profile.

Keywords

- Acute coronary syndromes
- Stents
- P2Y12 antagonists
- Thienopyridines
- Aspirin

Introduction

Guidelines recommend the use of dual antiplatelet therapy (DAPT), administered for 6–12 months after drug-eluting stent (DES) implantation for the prevention of coronary stent thrombosis and for a year after an acute coronary syndrome (ACS).\(^1,2\) Recently, important trials have shed light on strategies of DAPT in various clinical situations, and should impact the next rounds of international guidelines as well as routine practice.

When to start oral dual antiplatelet therapy in acute coronary syndrome patients?

NSTE-ACS

Treatment initiation with a P2Y\(_{12}\) receptor inhibitor, in addition to aspirin (and anticoagulation), upon presentation with a suspected NSTE-ACS comes from the CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Events) trial, which evaluated clopidogrel in the setting of primarily medical management of NSTE-ACS patients (Table 1).\(^3\) Clopidogrel reduced the risk of cardiovascular (CV) death, myocardial infarction (MI), or stroke by 20%.

Clopidogrel is a prodrug that needs to undergo metabolic transformation into its active metabolite and thus there was a concern that initiation of clopidogrel at the time of percutaneous coronary intervention (PCI) would not offer adequate antiplatelet therapy peri-PCI. Support for this concept came from a subgroup analysis of the CURE study. In the 21% of the study population who went on to PCI, those who had been randomized to clopidogrel upon presentation (and thus received clopidogrel ‘pre-treatment’ when compared with the control arm who received clopidogrel only starting with their PCI) had a 30% relative risk reduction of the composite endpoint of CV death, MI, and urgent target vessel revascularization at 30 days after PCI.\(^4\) However, it should be noted that the average time to catheterization was 10 days. Although subsequent studies yielded somewhat conflicting results (Table 1),\(^5–7\) the ACTION PCI meta-analysis of randomized controlled trials did show that clopidogrel pre-treatment reduced major coronary events by 23% (95\% CI 11–34%; \(P < 0.001\)), primarily driven by the reduction in peri-PCI MI. There was increased major bleeding, but no difference in all-cause mortality.\(^8\)

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However, neither CURE nor CREDO tested the question of pre-treatment as it would be applied today (i.e. treatment initiated before knowing the coronary status in patients managed invasively). In contrast, ACCOAST was the first randomized comparison of pre-treatment as it would be applied today (i.e. treatment initiated before knowing the coronary status in patients managed invasively). In the pre-treatment arm, prasugrel 30 mg was administered at the time of diagnosis and prasugrel 60 mg after diagnostic angiography only when PCI was planned. The ACTION NSTE-ACS meta-analysis of the three randomized studies evaluating pre-treatment showed a 21% reduction in MACE with clopidogrel pre-treatment, but no benefit with prasugrel and thus when combined an overall odd ratio (OR) for MACE of 0.87 (0.73–1.04) (Figure 1). There was a significant excess of bleeding complications without reduction in all-cause mortality. Similar findings were reported for the subgroup of NSTE-ACS patients who underwent PCI. Overall, whereas it might be reasonable to pre-treat with clopidogrel, important changes in the past decade including patients going for cardiac catheterization within hours rather than days and the introduction of more potent and faster acting P2Y12 receptor inhibitors, make briefly deferring administration of a P2Y12 receptor inhibitor until coronary anatomy is defined a reasonable option, especially when cangrelor is also now available for immediate P2Y12 blockade. One might consider extrapolating these data to ticagrelor, which, like prasugrel, also has a much faster onset of action and greater potency than clopidogrel. However, it should be acknowledged that the PLATO study that established the benefit of ticagrelor in NSTE-ACS (including a mortality benefit which may or may not be related to P2Y12 inhibition) initiated treatment upon presentation, so that all patients undergoing catheterization had been pre-treated with clopidogrel and/or ticagrelor, precluding any conclusion on the optimal timing of administration.

**STEMI**

Patients with STEMI have particularly hyperreactive platelets, have also a shorter time from diagnosis to angiography, and are more likely to undergo immediate PCI after angiography, all of which make it more challenging to fully inhibit platelets by the time of PCI.

### Table 1 Main randomized controlled trials of pre-treatment

<table>
<thead>
<tr>
<th>Study name</th>
<th>Population</th>
<th>No. of patients</th>
<th>Pre-treatment (timing)</th>
<th>No pre-treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>CURE 2001</td>
<td>NSTE-ACS</td>
<td>12,562 (PCI, n = 2658)</td>
<td>300 mg LD (median 10 days pre-PCI) then 75 mg MD for 3–12 months</td>
<td>No LD then 75 mg for 4 weeks if PCI</td>
<td>30 days</td>
</tr>
<tr>
<td>CREDO 2002</td>
<td>Stable/NSTE-ACS</td>
<td>2116</td>
<td>300 mg LD 3–24 h pre-PCI (mean 9.8 h) then long-term MD</td>
<td>No pre-treatment 28 days clopidogrel</td>
<td>28 days</td>
</tr>
<tr>
<td>PRAGUE-8 2008</td>
<td>Stable</td>
<td>1028</td>
<td>600 mg LD (&gt;6 h pre-PCI)</td>
<td>600 mg LD in cath-lab before PCI</td>
<td>7 days/hospital discharge</td>
</tr>
<tr>
<td>ARMYDAS 2010</td>
<td>Stable/NSTE-ACS</td>
<td>409</td>
<td>600 mg LD (4–8 h pre-PCI)</td>
<td>600 mg LD in cath-lab before PCI</td>
<td>30 days</td>
</tr>
<tr>
<td>ACCOAST 2013</td>
<td>NSTE-ACS</td>
<td>4033</td>
<td>Prasugrel 30 mg at admission Then, prasugrel 30 mg in cath-lab if PCI (median 4 h before catheterization)</td>
<td>Placebo at admission Then, prasugrel 60 mg in cath-lab if PCI</td>
<td>30 days</td>
</tr>
<tr>
<td>PCI CLARITY 2005</td>
<td>STEMI/ fibrinolysis + PCI</td>
<td>1863</td>
<td>300 mg LD at hospital presentation (median 3 days) then 75 mg MD</td>
<td>Placebo LD and MD 300 mg LD then 75 mg MD if PCI</td>
<td>30 days</td>
</tr>
<tr>
<td>CIPAMI 2011</td>
<td>STEMI/primary PCI</td>
<td>337</td>
<td>600 mg (timing unknown)</td>
<td>600 LD in cath-lab Open-label</td>
<td>7 days/hospital discharge</td>
</tr>
<tr>
<td>ATLANTIC 2014</td>
<td>STEMI/primary PCI</td>
<td>1862</td>
<td>Ticagrelor 180 mg LD (median 63 min pre-PCI)</td>
<td>Ticagrelor 180 mg LD (in-hospital) Double-blind</td>
<td>30 days</td>
</tr>
</tbody>
</table>

LD, loading dose; MD, maintenance dose.
With regard to clopidogrel, analogous to the analyses performed in CURE, the benefit of pre-treatment was examined within the context of CLARITY-TIMI 28 (Clopidogrel as Adjunctive Reperfusion Therapy – Thrombolysis In Myocardial Infarction 28), which was a randomized, double-blind, placebo-controlled trial of clopidogrel (300 mg loading dose followed by 75 mg daily) in patients receiving fibrinolytics for STEMI. In the subgroup of patients undergoing secondary PCI, clopidogrel pre-treatment compared with in-laboratory administration of clopidogrel reduced the composite outcome of cardiovascular death, recurrent MI, or stroke without a significant increase in major or minor bleeding. Subsequently, two small studies in patients undergoing primary PCI remained inconclusive. The ACTION PCI meta-analysis showed significant reductions in major ischaemic coronary events and of mortality with pre-treatment, and no increase in major bleeding in the STEMI subset.

Pre-hospital treatment with the potent P2Y12 inhibitor ticagrelor in patients with STEMI was tested in the ATLANTIC (Administration of Ticagrelor in the Cath Lab or in the Ambulance for New ST Elevation Myocardial Infarction to Open the Coronary Artery) study. A total of 1862 patients with STEMI were randomized to receive in a double-blind fashion a pre-hospital loading dose of ticagrelor or placebo at first medical contact. The placebo group received the loading dose of ticagrelor at the time of PCI in the catheterization laboratory. The median time difference between the two strategies was only 31 min. There were no differences between the two groups in terms of coronary reperfusion measured before PCI (primary endpoint). After PCI, there was no difference in the rate of MACE between the two arms, but the rate of definite stent thrombosis was lower in the pre-hospital group than in the in-hospital group. There was no difference in bleeding complications or side effects with the pre-hospital administration of ticagrelor.

In summary, in NSTE-ACS if treating with clopidogrel, initiation at the time of diagnosis would be consistent with how the drug was given in the pivotal study (i.e. with a conservative management or with several days of medical treatment before angiography). In these conditions, there are some data suggesting that pre-treatment may decrease major coronary events post-PCI. However, the guidelines now recommend prasugrel or ticagrelor over clopidogrel for patients with ACS. The design of the pivotal trial of prasugrel for this indication and the ACCOAST findings support initiation of prasugrel at the time of PCI and not upstream. Initiation upon diagnosis would be consistent with the pivotal trial for ticagrelor for this indication, although no study has examined ticagrelor pre-treatment in this setting. In STEMI, all the trials to date had initiation of the P2Y12 inhibitor at the time of diagnosis and the ATLANTIC trial suggests that initiation of ticagrelor pre-hospital may help reduce stent thrombosis. Thus, the benefit–risk of DAPT pre-treatment appears to depend on the type of ACS, the time until angiography, and the onset of action of the drug (Figure 2). The issue of pre-treatment may become moot with the availability of the intravenous P2Y12 inhibitor cangrelor.
When to stop dual antiplatelet therapy after an acute coronary syndrome?

Duration of dual antiplatelet therapy shorter than a year

Both American and European guidelines recommend the use of oral DAPT for 12 months after an ACS. This timing comes from the CURE trial, in which aspirin-treated patients with NSTE-ACS were randomized to clopidogrel treatment (300 mg loading dose followed by 75 mg/day) or placebo for 3 to 12 months with finally an average duration of 9 months. The duration of oral DAPT using clopidogrel was also evaluated in PCI-treated patients, some being ACS patients, recruited in the CREDO trial with a 27% relative reduction of the risk of death, MI, or stroke with 12 months vs. 28 days of post-procedural clopidogrel therapy. The duration of 12 months of DAPT was accepted, recommended, and reproduced in subsequent trials when more potent P2Y12 inhibitors were studied in NSTE-ACS.

In the pivotal studies for clopidogrel, prasugrel, and ticagrelor, landmark analyses all showed continued divergence of the ischaemic event curves beyond the first month of treatment, suggesting that treatment should be for at least 12 months, and raised the possibility (discussed below) that treatment beyond 12 months might lead to further reductions in ischaemic events. However, no randomized trial ever formally evaluated a duration of oral DAPT shorter than 12 months (e.g. 6 vs. 12 months). Some indirect evidence is provided from recent trials which evaluated the duration of treatment in stented patients when a majority of the patients enrolled were ACS patients. The PRODIGY, RESET, and EXCELLENT studies enrolled more than 5000 patients in total and had, respectively, 75, 55, and 51% of patients with ACS. There was no significant interaction between the duration of antiplatelet therapy (short vs. long) and clinical presentation (ACS vs. no ACS) for the primary endpoints of all three studies. In these studies, there was no substantial difference on ischaemic endpoints between short and long DAPT duration, but there tended to be more bleeding (Table 2). However, given the small numbers of events, these data are not definitive.

Duration of dual antiplatelet therapy longer than a year

As noted above, the continued divergence of the event curves in the landmark analyses from the 1-year NSTE-ACS trials suggested that prolonged P2Y12 inhibition beyond 1 year might be beneficial. Moreover, subgroup analyses of the CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance) trial in patients with documented arterial disease (prior MI, ischaemic stroke, or symptomatic peripheral arterial disease, n = 9478) and particularly in patients with prior MI (n = 3846) found significant reductions in the risk of CV death, MI, or stroke with the combination of low-dose aspirin plus clopidogrel compared with aspirin alone at 30 months [0.829, 95% CI (0.719–0.956) for patients with arterial disease and 0.774, 95% CI (0.613–0.978) for patients with prior MI]. Building on these observations, two dedicated studies have now shown that prolonged treatment with DAPT beyond 1 year in patients with an ACS does indeed significantly reduce ischaemic events.

The randomized, placebo-controlled DAPT trial evaluated the benefits and risks of continuing DAPT beyond 1 year after the placement of a coronary stent. At 12 months after DES implantation,
9961 patients who had not had a major ischaemic or bleeding event and had been adherent to DAPT were assigned to continue thienopyridine (about two-thirds were on clopidogrel and one-third on prasugrel) and aspirin treatment or to receive placebo plus aspirin for the next 18 months. Overall, continuing thienopyridine reduced the rates of both co-primary endpoints, stent thrombosis (HR 0.29, 95% CI 0.17–0.48, 0.4 vs. 1.4%, \(P\), 0.001) and death, MI, or stroke (HR 0.71, 95% CI 0.59–0.85, 4.3 vs. 5.9%, \(P\), < 0.001). Interestingly, the reduction of MI was approximately as frequent in lesions within the stented artery as in non-stented arteries, suggesting a secondary prevention effect of the strategy of prolonged DAPT. Continued thienopyridine increased the rate of moderate or severe bleeding (2.5% vs. 1.6%, \(P\) = 0.001). An increased risk of stent thrombosis and MI was observed during the 3 months after stopping thienopyridine, adding to the demonstration of long-term ischaemic protection with DAPT.

Within the DAPT trial, 43% of the study population was stented for an ACS. In this large subgroup, there were even clearer signs of

<table>
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<th>Table 2</th>
<th>Endpoints in studies evaluating abbreviated duration of dual antiplatelet therapy (6 months or less) after stenting in populations having a majority of acute coronary syndrome patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Stent thrombosis</td>
</tr>
<tr>
<td></td>
<td>S-DAPT</td>
</tr>
<tr>
<td>PRODIGY</td>
<td>15 (1.5)</td>
</tr>
<tr>
<td>RESET</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>EXCELLENT</td>
<td>6 (0.9)</td>
</tr>
<tr>
<td>Total n/N (%)</td>
<td>23/2532 (0.9)</td>
</tr>
</tbody>
</table>

Results reported as n (%). MACE was defined as death, MI, or stroke in PRODIGY, death, MI, or stent thrombosis in RESET, death, MI, stroke, or urgent revascularization in EXCELLENT.

L-DAPT, long dual antiplatelet therapy; MI, myocardial infarction; S-DAPT, short dual antiplatelet therapy.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Main studies evaluating long-term duration of dual antiplatelet therapy in coronary patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies</td>
<td>Drug</td>
</tr>
<tr>
<td>CHARISMA</td>
<td>Clopidogrel</td>
</tr>
<tr>
<td>DES-late</td>
<td>Clopidogrel</td>
</tr>
<tr>
<td>PRODIGY</td>
<td>Clopidogrel</td>
</tr>
<tr>
<td>ARCTIC-interruption</td>
<td>Clopidogrel or prasugrel</td>
</tr>
<tr>
<td>DAPT</td>
<td>Clopidogrel or prasugrel</td>
</tr>
<tr>
<td>TRILOGY</td>
<td>Prasugrel (vs. clopidogrel)</td>
</tr>
<tr>
<td>PEGASUS-TIMI 54</td>
<td>Ticagrelor 90 or 60 mg bid (vs. placebo)</td>
</tr>
<tr>
<td>TRACER</td>
<td>Vorapaxar (vs. placebo)</td>
</tr>
<tr>
<td>TRA-2P</td>
<td>Vorapaxar (vs. placebo)</td>
</tr>
</tbody>
</table>
Recent trials on DAPT

benefit with an HR of 0.56 (95% CI 0.42–0.76, 3.9 vs 6.8%, \( P < 0.001 \) for death, MI, or stroke (Figure 3), with a directionally consistent effect on cardiac death (HR 0.67, 95% CI 0.31–1.44) and no excess of non-cardiovascular death.\(^{25} \)

The largest study examining the role of DAPT in coronary patients beyond 1 year is the PEGASUS-TIMI 54 trial.\(^{26} \) This randomized double-blind trial evaluated the efficacy and safety of ticagrelor in addition to low-dose aspirin for long-term treatment of 21,162 stable patients with a history of spontaneous MI 1–3 years before randomization. PEGASUS-TIMI 54 evaluated two intensities of antiplatelet therapy using the 90 mg twice daily dose of ticagrelor previously studied as well as a lower dose, 60 mg twice daily and followed up patients for a median of 33 months. Both doses of ticagrelor reduced the risk of cardiovascular death, MI, or stroke compared with placebo, with an HR of 0.85 (95% CI 0.75–0.96, 7.85 vs. 9.04%, \( P = 0.008 \)) for the 90 mg dose and an HR of 0.84 (95% CI 0.74–0.95, 7.77 vs. 9.04%, \( P = 0.004 \)) for the 60 mg dose (Figure 3). There was consistency in the effects on the individual components of the composite endpoint, with HRs (95% CI) of 0.85 (0.71–1.00), 0.83 (0.72–0.95), and 0.78 (0.62–0.98) for CV death, MI, and stroke for the pooled ticagrelor doses vs. placebo. Both doses increased the risk of TIMI major bleeding (2.6, 2.3, and 1.1% respectively), but the rates of fatal bleeding or non-fatal intracranial haemorrhage did not differ significantly between either ticagrelor dose group and placebo. The rates of bleeding and other side effects such as dyspnoea were numerically lower with the 60-mg dose of ticagrelor than with the 90-mg dose, resulting in a lower rate of discontinuation of the study drug and a better safety and tolerability profile with the 60-mg dose. There was a trend with ticagrelor 60 mg bid towards a reduction in death from any cause, but this effect was not significant. For every 1000 patients started on ticagrelor 60 mg bid, over 3 years 13 major ischaemic events (cardiovascular death, MI, or stroke) per year would be prevented at the cost of nine TIMI major bleeding, with no excess in fatal bleeding or intracranial bleeding.\(^{25} \) Put another way, the number needed to harm to cause a major bleed is 79.

There are also two other trials that suggest more prolonged intensive antiplatelet therapy after ACS reduces ischaemic events. The TRILOGY-ACS (TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medicallY manage Acute Coronary Syndromes) double-blind, randomized trial evaluated up to 30 months of treatment with prasugrel or clopidogrel after a coronary event in patients receiving medical therapy without planned revascularization.\(^{27} \) Prasugrel did not significantly reduce the frequency of the primary ischaemic endpoint, when compared with clopidogrel, and similar risks of bleeding were observed. However, after 1 year the event curves start to diverge and a significant reduction was seen. This effect was even more pronounced in patients who had angiography and thereby had confirmed significant coronary disease.\(^{28} \) (Figure 3).

In TRA 2P-TIMI 50 trial (Thrombin Receptor Antagonist in Secondary Prevention of Atherothrombotic Ischemic Events (TRA 2P)—Thrombolysis in Myocardial Infarction (TIMI) 50 trial),\(^{29} \) vorapaxar, a protease-activated receptor 1 inhibitor (a major thrombin receptor on platelets), reduced the risk of death, MI, or stroke in patients with prior MI (\( n = 17,779 \)) compared with the placebo group, in addition to standard therapy, at 36-month follow-up\(^{30} \) (Figure 3). In landmark analyses, more intensive antiplatelet therapy reduced events both in the first year of treatment as well as beyond 1 year to 36 months, with the event curves continuing to diverge.

Figure 3 Results of the five studies which tested stronger antiplatelet therapy beyond 1 year vs. standard of care, in patients with proven coronary artery disease (prior myocardial infarction or angiographically proven coronary artery disease).
The current 1-year recommendation for DAPT is simply a function of the duration of the pivotal trials for P2Y12 inhibitors in ACS. Landmark analyses from those trials had suggested continued benefit with prolonged therapy as had the MI subgroup analysis from a dedicated trial of long-term P2Y12 inhibition. Prospective data from DAPT and PEGASUS-TIMI 54 now confirm the benefit of prolonged DAPT to prevent MACE in patients with ACS. This benefit occurs at the cost of more bleeding complications, but no excess of intracranial or fatal bleeding. Prolonged DAPT is most logical when the diagnosis of obstructive coronary artery disease is manifest (i.e. documented spontaneous MI, typically with confirmed CAD on angiography) and when there are no bleeding contraindications.

When to stop dual antiplatelet therapy after stenting in non-acute coronary syndrome patients?

The recent recommendations have been rather uniform for stented patients with or without ACS, considering 1 year as the optimal DAPT duration after implantation of a DES. However, the risk of stable patients differs from the risk of ACS patients after stenting and hospital discharge. Seven randomized trials have evaluated a duration of DAPT shorter than a year after stenting with DES in populations mostly constituted of stable CAD patients and, several meta-analyses have now been published. All the individual studies suffer from limitations including lack of power to detect differences in hard endpoints, open-label designs, wide non-inferiority margins, selection biases, premature interruption of several studies, treatment cross-over, low event rates and possibly underreporting of events, high percentage of patients lost to follow-up, and heterogeneous primary endpoints across studies.

In terms of treating for longer than 12 months, the largest experience comes from the DAPT trial, in the subgroup of patients without prior MI, the HR for stent thrombosis was 0.33 (95% CI 0.18–0.60) and for MACE was 0.83 (95% CI 0.68–1.02), with a statistically significant reduction in MI (HR 0.60, 95% CI 0.45–0.79) (Table 3). Of note, though, in patients treated with everolimus-eluting stents, the absolute risk difference for MACE was modest (4.3 vs. 4.5%). The protective effect of long-term DAPT was also found to be attenuated with the use of second-generation DES in a recent meta-analysis. In DAPT, a borderline increase in all-cause mortality was observed with continued thienopyridine (2.0%) vs. placebo (1.5%, P = 0.052), and this risk appeared to be seen just in the patients with stable ischaemic heart disease and not in those with ACS. The excess of deaths was driven by an increase in non-cardiovascular deaths. Imbalances were seen in bleeding and cancer; although the biological plausibility for the latter is unclear. The relevance of this finding on mortality remains controversial across different PCI studies and meta-analyses, some suggesting harm with prolonged DAPT after stenting, others not confirming the harm associated with prolonged DAPT.

Accordingly, a short mandatory period of DAPT of ~6 months could be considered for optimal safety and acceptable efficacy in non-ACS patients undergoing PCI with the latest-generation DES, when patients are considered at risk of bleeding. If the bleeding
Conclusions
Dual antiplatelet therapy improves cardiovascular outcomes after ACS and/or PCI. Recent clinical trials have provided important new information allowing for evidence-based decisions regarding timing of initiation, intensity of antiplatelet therapy, and duration of treatment. In stable patients undergoing PCI with the latest-generation DESs, patients should be treated for at least ~6 months. A shorter course of therapy may be necessary during special situations (e.g., surgery; oral anticoagulation—Figure 4). Longer courses of therapy may be reasonable in patients at low bleeding risk who are tolerating DAPT well. For patients with ACS, prolonged DAPT is beneficial and therefore reasonable as long as the patient is tolerating the therapy. Ideally further research will facilitate optimal individualized management of DAPT, which must be seen as a dynamic prescription with regular re-evaluations of the benefit—risk to the patient according to changes in his/her clinical profile.

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References


