

# Dual antiplatelet therapy: short or long after acute coronary syndrome?

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## WHAT THE GUIDELINES SAY

According to the latest ESC guidelines for the treatment of acute coronary syndrome (ACS) patients (1) treatment recommendations are as follows:

Aspirin (acetylsalicylic acid) is recommended for all ACS patients without contraindications. The initial oral loading dose (LD) is 150–300 mg in aspirin-naïve patients, the maintenance dose (MD) is 75–100 mg/day. Aspirin is usually combined with a P2Y12-inhibitor, whereby prasugrel (60 mg LD or ticagrelor are preferred over clopidogrel unless these stronger antiplatelet agents are not available or contraindications exist. The recommended duration for dual antiplatelet therapy (DAPT) after ACS is 12 months, independent of the initial treatment strategy, which is either conservative medical treatment only, percutaneous coronary intervention (PCI), or bypass surgery, respectively. (1, 2)

Key words: clopidogrel, prasugrel, ticagrelor, dual antiplatelet therapy

## PROLONGED DAPT

DAPT beyond 1 year may be considered in patients with high-risk for future ischemic events after careful assessment of the individual bleeding risk. This recommendation is mainly based on the results of the DAPT Trial (aspirin plus clopidogrel or prasugrel prolongation) (3) or the PEGASUS trial (aspirin plus ticagrelor prolongation). (4) In both trials the risk of ischemic events was reduced on longer- versus shorter term DAPT treatment. However, both trials demonstrated an overall increase of bleeding hazards. Accordingly, the se-

lection of patients who are suitable for prolonged DAPT has to be exact on an individual basis. Figure 1 offers suggestions for patient selection with respect to a prolonged DAPT when the bleeding risk is normal or only moderately increased. It is furthermore recommended to use medical strategies for gastric protection in patients undergoing prolonged DAPT.

## SHORTENED DAPT

A shorter duration (3–6 months) may be in patients at high bleeding risk (Figure 1) as bleeding complications occur the more frequent, the longer DAPT is performed and as bleeding is a major predictor of an adverse prognosis including all-cause death.

Shorter DAPT duration after ACS usually lasts between 3 and 6 months depending on the patients' individual situation. In some ACS patients with an increased bleeding risk who undergo PCI even the 3–6 months of DAPT seems too long. In such patients the use of second-generation

drug eluting stents might allow an even shorter DAPT of only 1 month with a switch to antiplatelet mono-therapy thereafter. This has been tested in the prospective randomized LEADERS trial with a biolimus-eluting stent (6) and in the retrospective analysis of the ZEUS trial by use of a zotarolimus-eluting stent. (7) In both trials the respective DES was superior to the compared bare metal stents<sup>1</sup>, which have been recommended in such situations before.

## SKIPPING ASPIRIN

Based on the knowledge that thrombo-embolic complications after successful PCI in stable/elective but also in ACS patients occur preferably within in the first 3 months after the intervention, two trials currently investigate DAPT with aspirin and ticagrelor only for 1 month (GLOBAL LEADERS trial, GL) or for 3 months (TWILIGHT trial, TW) followed by mono-therapy with the P2Y12-inhibitor only. Results may be expected in 1 (GL)

## DAPT <= 12 Months

History of bleeding  
History of hemorrhagic stroke  
Increased bleeding risk (by bleeding scores)  
Chronic therapy with oral anticoagulants  
Chronic therapy with NSARs  
Chronic kidney disease (stage IV-V)  
Frailty  
Malignancy

## DAPT > 12 Months

History of stent thrombosis  
History of myocardial infarction  
Complex coronary anatomy  
Diabetes mellitus  
Peripheral artery disease  
Chronic kidney disease (stages I-III)

Figure 1. Adapted after Weiss et al. (5)  
NSAR, nonsteroidal anti-inflammatory drug

to 3 (TW) years from now. In both trials patients with the need for chronic oral anticoagulation are excluded.

### THE CHOICE OF THE CORRECT P2Y12-INHIBITOR IN DAPT

In opposite to ESC guidelines, a considerable percentage of patients are currently not treated with the more potent P2Y12-inhibitors worldwide, but received clopidogrel, either because prasugrel or ticagrelor are not available, but frequently also despite missing contraindications against prasugrel or ticagrelor. The percentage of clopidogrel users in ACS patients prior to, during or after PCI varies between 10% (Sweden) and 40% (Germany). Thereby, the most causal factors for the initial pre-

scription of clopidogrel are fear from bleeding due to age and/or co-morbidities associated with bleeding for both stronger P2Y12-inhibitors, or in case of ticagrelor only, with dyspnea and bradycardia. In a recent investigation of inappropriate clopidogrel use in ACS patients in Austria (ATTAIN registry) (8) 27,2 % of patients received clopidogrel at hospital discharge but 55,2 of those had no contraindication against prasugrel or ticagrelor. Of importance was the finding that an active switch from initially used clopidogrel to a stronger P2Y12-inhibitor in-hospital only takes place in a very low percentage of patients. This situation may be similar in other countries and demands improvement in order to follow guideline recommendations.

### CONCLUSION

DAPT in secondary prevention after ACS should be performed with aspirin plus prasugrel (after the knowledge of the coronary anatomy and the need for PCI) or with aspirin plus ticagrelor independent of treatment strategy (conservative, or PCI, or surgery). Clopidogrel should only be used in case of contraindications against the stronger P2Y12-inhibitors or in case these agents are not available. Duration of DAPT lasts usually 12 months but shorter or longer DAPT depends on weighing ischemic and bleeding risk of the respective patient and should be decided on an individual basis.

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