Assessing the most appropriate duration of dual antiplatelet therapy after coronary stenting

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A randomised multicentre open-label study evaluating the efficacy and safety of prolonged antiplatelet therapy in patients with coronary disease has found that 24 months' duration of dual therapy is no better than six months DAPT in preventing adverse cardiac events.

However, the PROlonging Dual antiplatelet treatment after Grading stent-induced Intimal hyperplasia studY (PRODIGY) also found a consistently greater risk of haemorrhage in the 24-month dual therapy group according to all prespecified bleeding definitions, including the recently proposed Bleeding Academic Research Consortium classification. The need for transfusion was also increased in the longer treatment group.

The results, said investigator Dr Marco Valgimigli from the University Hospital of Ferrara, Italy, "question the validity of current guideline recommendations - which were based on registry data - that at least 12 months' dual antiplatelet therapy should be pursued after implantation of a drug-eluting stent.

"While we cannot exclude the possibility that a smaller than previously anticipated benefit may still exist in prolonging therapy with clopidogrel for several months after coronary stenting, our study clearly shows that the benefit to risk ratio of prolonged therapy has been over-emphasised."

The PRODIGY study was a 4-by-2 randomised, three-centre open-label

clinical trial designed to assess the efficacy and safety of prolonged clopidogrel therapy for up to 24 months in all-comer patients receiving a balanced combination of drug-eluting stents (with various anti-intimal hyperplasia potency and belonging to both first and second generation). Patients were 18 years or older with chronic stable coronary artery disease or acute coronary syndromes, including non-ST-elevation and ST-elevation myocardial infarction.

More than 2000 patients scheduled for elective, urgent or emergency coronary angioplasty were randomly assigned in a 1:1:1:1 fashion to one of four stent types: everolimus-eluting stent, paclitaxel-eluting stent, zotarolimus-eluting stent or third-generation thin-strut bare metal stent. Randomisation to the four different types, said Dr Valgimigli, was justified by the different safety profile of each, which was meant to ensure that patients in the two main study groups (six versus 24 month dual antiplatelet therapy) received exactly the same stent types. At 30 days, patients in each stent group were then further randomised to either six or 24 months of dual antiplatelet treatment.

The primary objective of the study was to assess whether 24-month dual antiplatelet treatment, consisting of clopidogrel and aspirin after coronary stenting, was associated with a lower cumulative incidence of all-cause mortality, non-fatal myocardial infarction or cerebrovascular accident (the primary outcome) than six-month dual therapy.

Results showed that the cumulative risk of the primary outcome at two years was 10.1% with the 24-month treatment, and 10.0% with the six-month (HR 0.98; 95% CI 0.74-1.29; P=0.91). The individual risks of death, myocardial infarction, cerebrovascular accident or stent thrombosis did not differ between the two groups.

Among the patients receiving long-term dual antiplatelet therapy, there was a roughly two-fold greater risk of type 5, 3 or 2 bleeding events (HR

2.17, 95% CI 1.44-3.22; p=0.00018) as well as type 5 or 3 bleeding events (HR 1.78, 95% CI 1.02-3.13; p=0.037) according to the Bleeding Academic Research Consortium classification. The risks of TIMI-defined major bleeding and red blood cell transfusion were also increased in the 24-month clopidogrel group.

Commenting on the implications of the results, Dr Valgimigli said: " While a formal economic analysis will follow, the results of this study have important implications for heathcare expenditure - for this study shows that prolonging therapy with clopidogrel beyond six months is not only associated with no clinical benefit but also with a significant increase in actionable bleeding events requiring re-hospitalisations and multiple diagnostic and therapeutic resources."

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