Clopidogrel optimal loading dose Usage to Reduce Recurrent EveNTs-Organization to Assess Strategies in Ischemic Syndromes – CURRENT OASIS 7

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Another important trial that was presented at the European Congress of Cardiology, held in Barcelona in September 2009, in the Interventional Cardiology Topics, was Clopidogrel optimal loading dose Usage to Reduce Recurrent EveNTs-Organization to Assess Strategies in Ischemic Syndromes – CURRENT OASIS 7.

The aims of the study was to assess the safety and efficacy of a high daily dose of aspirin compared to a low dose of aspirin, and also to compare standard dose of clopidogrel with double dose of clopidogrel, among patients with ST or non–ST-segment elevation acute coronary syndrome (ACS). Over 20,000 of patients with with unstable angina, NSTEMI or STEMI, were randomized to a clopidogrel high dose regimen (600 mg loading dose, then 150 mg once daily on days 2-7, followed by 75 mg once daily on days 8-30) compared to the standard regimen, and also were randomized to a highly dose of aspirin (300-325 mg) or to a low dose of aspirin (75-100mg). All patients were followed for 30 days. The primary endpoints included data of efficacy – CV death, myocardial (re) infarction, or stroke up to 30 days, and data of safety – major bleeding. PCI was done in 70% of the patients.

Trial results showed that there was a significant interaction between low dose and high dose aspirin and standard dose and double dose clopidogrel (p=0.043). In the high dose aspirin group, the primary efficacy event rate was lower in the double dose clopidogrel vs the standard dose clopidogrel group (4.6% vs 3.8%, RR 0.83, 95% CI 0.70-0.99, p=0.036). However, there was no difference between the double dose clopidogrel vs the standard dose clopidogrel group in the low dose aspirin cohort (4.2% vs 4.5%, RR 1.07, 95% CI 0.91-1.27, p=0.42). The interaction between aspirin dose and clopidogrel dose did not reach statistical significance for the composite endpoint of MI/stent thrombosis (p=0.19) or major bleeding (p=0.099).

There was no difference in the primary endpoint of CV death, MI or stroke at 30 days

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between the low and high dose aspirin groups (4.4% vs 4.2%, p=0.76). The lack of difference was consistent in the PCI cohort (4.2% for low dose aspirin vs 4.1% for the high dose group, p=0.76) and the no PCI cohort (4.7% vs 4.4%, p=0.44). Likewise, there was no difference in stent thrombosis between low dose aspirin (2.1%) and high dose aspirin (1.9%). The primary safety endpoint of trial-defined major bleeding occurred in 2.3% of patients in both aspirin groups and severe bleeding occurred in 1.7% of each group.

Furthermore, when compared standard vs double dose of clopidogrel, there was no difference in the primary endpoint of CV death, MI or stroke at 30 days (4.4% for standard dose vs 4.2% for double dose). On the other hand, there was a significant interaction with performance of PCI (p-interaction=0.016), with a lower rate of the primary endpoint with double dose clopidogrel vs standard dose clopidogrel in the PCI cohort (4.5% vs 3.9%) In the PCI population, stent thrombosis was significantly lower in the double dose clopidogrel group (2.3% vs 1.6%).

In conclusion, this trial showed that among patients with ST or non–ST-segment elevation ACS, there was a significant interaction between aspirin dose and clopidogrel dose in the composite endpoint of CV death, MI, or stroke at 30 days, with no difference seen between double and standard dose clopidogrel in the low dose aspirin cohort and a significant reduction with double dose clopidogrel in the high dose aspirin cohort. When the factorial data were pooled, treatment with high dose aspirin was not associated with a difference in the composite endpoint of CV death, MI, or stroke at 30 days compared with low dose aspirin. Likewise, a double dose of clopidogrel was also not associated with a reduction in the primary endpoint compared with standard dose clopidogrel.

Other important finding was a reduction in the primary endpoint with double dose clopidogrel in the PCI cohort but no difference in the no PCI cohort. Trial-defined major bleeding, the primary safety endpoint of the trial, was more frequent with double dose clopidogrel compared with standard dose clopidogrel both overall and in the PCI cohort, but probably not in the no PCI cohort (data not reported). ❑