

TAXUS Landmark Analysis on Long-Term Clopidogrel Use

Extending thienopyridine use beyond one year after stent implantation does not appear to impact outcomes, according to data from the TAXUS landmark analysis presented at the Transcatheter Cardiovascular Therapeutics Symposium.¹ Gregg Stone, MD and colleagues examined 2,171 patients in the TAXUS II, IV, and V trials who received either bare metal stents (BMS) or drug-eluting stents (DES) and who were free of death, myocardial infarction (MI), total vessel revascularization (TVR) or stent thrombosis at one year. Participants received either a thienopyridine or no thienopyridine and were observed for 5 years.

Slightly more than half of participants were still taking thienopyridines at 5 years. Thienopyridine use did not significantly impact the rates of death, MI, or stent thrombosis at 2 years or at 5 years (Fig. 1). The authors reached several conclusions: 1) that patients taking thienopyridines at one year were more likely to remain on them at 5 years; 2) patients taking thienopyridines at one year tended to have fewer safety events through 5 years, although this did not reach statistical significance; 4) there may be benefit in high-risk groups that were not examined in this study; and 5) this study does not offer clear evidence for extending thienopyridine use beyond one year post-stenting.

The Best Time to Initiate Loading Dose of Clopidogrel: ARMYDA-5

Germano Di Sciascio, MD presented results of the ARMYDA-5 trial, which examined the best time to initiate a 600 mg loading dose of clopidogrel at TCT 2007.² ARMYDA-5 randomized 438 patients with stable angina or NSTEMI ACS to receive a 600 mg loading dose of clopidogrel either 4 to 8 hours before PCI or at the time of PCI, and examined the 30-day incidence of death, myocardial infarction, target vessel revascularization (primary end point), and markers of myocardial injury, platelet reactivity, and bleeding complications (secondary end points). Blood was drawn before PCI and at 8 and 24 hours post-PCI.

There was no significant difference in the primary end point between groups (8% of the pre-treatment group vs 11% of the in-lab group). There were no deaths or target vessel revascularizations—the occurrence of the primary end point was entirely from myocardial infarction. There was also no significant difference between groups in creatine kinase-MB (31% of pre-load vs 33% of in-lab patients) or troponin levels after PCI (39% of pre-load vs 47% of in-lab patients). Bleeding complications were minor and did not differ between groups. Platelet reactivity, as measured by VerifyNow™, was lower in the pre-load group at study entry (223 platelet reaction units [PRU]) than in the in-lab group (245 PRU). The difference remained at two hours post-PCI (241 PRU vs 272 PRU, respectively). However, at 6 and 24 hours, there was no difference in platelet reactivity between groups. The authors believe that in-lab clopidogrel is safe and can be effective; this may be particularly important in cases where the coronary anatomy is not known.

No Benefit Observed with Clopidogrel Double Loading Dose in ARMYDA-4

Germano Di Sciascio, MD and colleagues found that a 600 mg loading dose of clopidogrel administered pre-PCI may not confer additional benefit in patients already taking clopidogrel in the ARMYDA-4 study that was presented at Transcatheter Cardiovascular Therapeutics (TCT) 2007.³ Dr. Di Sciascio and colleagues examined the rate of the primary end point (30-day death, MI, or TVR) in 464 stable angina or non-ST elevation acute coronary syndrome (NSTEMI ACS) patients already taking clopidogrel therapy and undergoing PCI. Patients were randomized to receive either a 600 mg loading dose of clopidogrel at 4 to 8 hours pre-PCI (reload group) or placebo, in addition to their chronic therapy.

At 30 days, there was little difference between groups in the rate of the primary end point (7% of placebo patients versus 8% of the reload group; $P = 0.96$). There was also little difference between groups in the secondary end points—post-procedural elevation of creatine kinase-MB (27% in the re-load group vs 30% in the placebo group; $P = 0.58$) and troponin-1 levels (45% in the reload group vs 46% in the placebo group; $P = 0.98$). The rate of minor bleeding was equal between groups, at 4%. Additionally, platelet aggregometry did not show a significant difference in platelet reactivity between groups. These results indicate that patients taking chronic clopidogrel therapy can safely undergo PCI without the need for a loading dose of clopidogrel.

References

1. Stone GW, Ellis SG, Colombo A, et al. TAXUS landmark analysis. Impact of long-term clopidogrel usage on death, myocardial infarction and stent thrombosis. Presented at: Transcatheter Cardiovascular Therapeutics (TCT); October 23, 2007; Washington, DC.
2. Di Sciascio G, for the ARMYDA-5 Investigators. ARMYDA-5 (Antiplatelet therapy for Reduction of Myocardial Damage during Angioplasty) Study. Prospective, multicenter, randomized trial investigating influence on outcome of in-lab 600 mg clopidogrel loading vs 6-hour pre-PCI treatment-“ARMYDA-Preload”. Presented at: Transcatheter Cardiovascular Therapeutics (TCT); October 23, 2007; Washington, DC.
3. Di Sciascio G, for the ARMYDA-4 Investigators. ARMYDA-4 (Antiplatelet therapy for Reduction of Myocardial Damage during Angioplasty) Study. Prospective, multicenter, randomized, double blind trial investigating influence on PCI outcome of additional 600 mg clopidogrel load in patients on chronic therapy-“ARMYDA-RELOAD”. Presented at: Transcatheter Cardiovascular Therapeutics (TCT); October 23, 2007; Washington, DC.

Figure 1. Two- and Five-Year Rates of Death, MI, and Stent Thrombosis in the TAXUS Analysis

2-year events (Death, MI, or Stent thrombosis)	Hazard Ratio (HR) [95% Confidence Interval (CI)]	Rate (%)		P Values
		T+	T-	
DES	1.11 [0.47, 2.63]	1.8%	1.9%	0.82
BMS	0.76 [0.33, 1.74]	2.5%	1.9%	0.51
5-year events (Death, MI, or Stent thrombosis)				
DES	1.07 [0.70, 1.65]	8.3%	9.8%	0.75
BMS	1.31 [0.80, 2.12]	7.9%	9.2%	0.28

BMS = bare metal stent; DES = drug-eluting stent; MI = myocardial infarction; T = thienopyridine.

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