TL-PAS Shows Reduction of Ischemic Events With Long-term Prasugrel

Written by Muriel Cunningham

The results of the multicenter TAXUS Liberté Post Approval Study [TL-PAS; Garratt KN et al. *Circulation*. 2014] were presented by Kirk Garratt, MD, Lenox Hill Hospital, New York, New York, USA. Patients randomized in this prospective open-label study were also participants in the Dual Antiplatelet Therapy Study [Mauri L et al. *New Eng J Med*. 2014]. While the TL-PAS was not powered to show a difference in the end point analyses, the results from this specific trial were presented.

Eligible patients had a TAXUS Liberté paclitaxel-eluting stent placed and then took open-label aspirin plus prasugrel for 12 months after the index procedure [Garratt KN et al. *Circulation*. 2014]. At the end of 12 months, patients were randomized to blinded prasugrel (30-month group) or placebo (12-month group) plus open-label aspirin for another 18 months. Thirty months after the index event, blinded study medication was stopped, and the patients took aspirin for ≥ 3 months.

The co–primary efficacy end points were the occurrence of major adverse cardiac and cerebrovascular events (defined as the composite of death, myocardial infarction [MI], or stroke) and stent thrombosis (ST) occurring between 12 and 30 months after the index procedure. The primary safety end point was major bleeding occurring between 12 and 30 months after the index procedure (defined as *moderate* or *severe* by GUSTO criteria).

Of the 2191 randomized patients, about 75% were men, and the mean age was approximately 59 years; >96% were aged < 75 years and weighed > 60 kg.

At 540 days after randomization, patients in the 30-month prasugrel group had a significantly lower rate in the co–primary composite end point of death, MI, or stroke when compared with the 12-month group (Figure 1). This difference was also significant at the 90-day postrandomization

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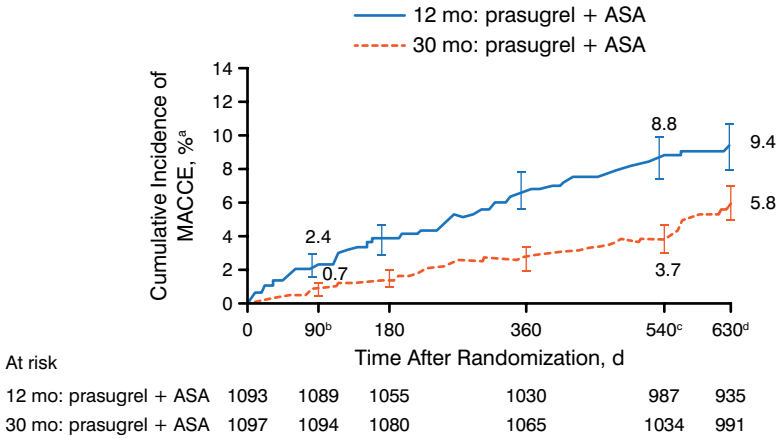
Figure 1. Co–Primary End Point: Major Adverse Cardiac and Cerebrovascular Events at 540 Days



ASA, acetylsalicylic acid (aspirin); MACCE, major adverse cardiac and cerebrovascular event.

[a]± 1.5 SE.

[b]HR, 0.303; 95% CI, 0.137 to 0.670; *P* = .002.

[c]HR, 0.407; 95% CI, 0.281 to 0.589; *P* < .001.

[d]HR, 0.591; 95% CI, 0.431 to 0.811; *P* < .001.

Adapted from Garratt KN et al. Prasugrel plus aspirin beyond 12 months is associated with improved outcomes after Taxus Liberté paclitaxel-eluting coronary stent placement. *Circulation*. 2015. E-pub ahead of print. DOI: 10.1161/CIRCULATIONAHA.114.013570. Accessed December 10, 2014. With permission from American Heart Association, Inc.

Table 1. Key TL-PAS Results at 540 Days Postrandomization

Events	Prasugrel Plus Aspirin, %		HR (95% CI)	Log-rank *P*
	12 mo	30 mo		
MACCE	8.8	3.7	0.407 (0.281 to 0.589)	< .001
Death	2.0	1.9	0.942 (0.511 to 1.739)	.850
Stroke	0.7	0.6	0.847 (0.285 to 2.521)	.765
MI	7.1	1.9	0.255 (0.156 to 0.417)	< .001
Definite/probable ARC ST	2.9	0.2	0.063 (0.015 to 0.264)	< .001
MI related to ST				
Yes	2.6	0.0	0.00 (0.000 to NA)	< .001
No	4.5	1.9	0.407 (0.242 to 0.686)	< .001
Major bleeding	1.7	2.4	1.438 (0.788 to 2.622)	.234
GUSTO				
Moderate bleed	1.2	2.1	1.759 (0.891 to 3.472)	.099
Severe bleed	0.5	0.3	0.594 (0.142 to 2.485)	.471

ARC, Academic Research Consortium defined; MACCE, major adverse cardiac and cerebrovascular event; MI, myocardial infarction; NA, not applicable; ST, stent thrombosis; TL-PAS, TAXUS Liberté Post Approval Study.

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time point ($P = .002$). The co–primary end point of ST was also lower in patients taking prasugrel for 30 months versus the 12-month group.

There were no significant differences in the rates of stroke or death, but patients in the 30-month group had significantly fewer MIs ($P < .001$). An increase in major bleeds was observed with prolonged prasugrel therapy, but the increase was not statistically significant, and the rate of severe bleeds was not higher in the 30-month treatment group. An important finding was that stopping prasugrel appeared to result in a loss of protection, as an increase in ischemic events was seen within 90 days of discontinuation in both arms. Key effectiveness and safety study results are presented in Table 1.

Dr Garratt noted that the trial has several limitations. Patients with a history of prior cerebrovascular or active bleeding events were excluded, and those patients who were randomized had demonstrated tolerance to prasugrel for 12 months. In addition, elderly patients or those with a lower body mass may have been underrepresented. However, these data demonstrate that long-term prasugrel reduces ischemic events while increasing the risk of bleeding. Furthermore, these data provide additional evidence that cessation of antiplatelet agents increases the short-term risk of ischemic events during the period immediately following cessation of therapy.

ITALIC/ITALICplus: 12-Month Data Suggest 6 Months of DAPT Is Noninferior to 24 Months of DAPT

Written by Muriel Cunningham

The Is There a Life for Drug Eluting Stent (DES) After Discontinuation of Clopidogrel trial [ITALIC/ITALICplus; Gilard M et al. *J Am Coll Cardiol*. 2014] was a large, prospective, open-label randomized trial conducted at 55 sites in Europe and the Middle East. The objective of the trial was to determine if 6 months of dual antiplatelet therapy (DAPT) was noninferior to 24 months of DAPT following drug-eluting stent (DES) placement. Martine Gilard, MD, PhD, Brest University, Brest, France, presented the 12-month results of the ITALIC/ITALICplus trial.

Eligible patients had at least one Xience V DES placed and were pretreated with aspirin plus clopidogrel, prasugrel, or ticagrelor. Patients were not pretreated with abciximab during their hospital stay.

Patients were excluded if they had platelets < 100 000/µl, known hemorrhagic diathesis, major surgery during the previous 6 weeks or any scheduled during the year after enrollment, evidence of active gastrointestinal or urogenital bleeding, severe liver failure, a severe medical