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.

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.

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

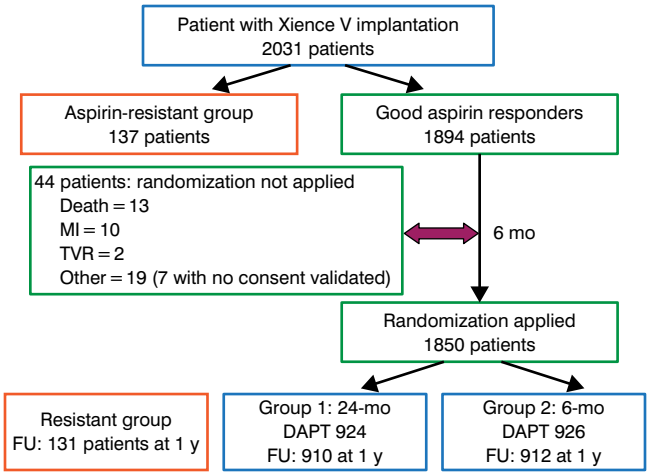
Written by Muriel Cunningham

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

Figure 1. Study Design and Patient Flow



DAPT, dual antiplatelet therapy; FU, follow-up; MI, myocardial infarction; pts, patients; TVR, target vessel revascularization.

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condition with a life expectancy < 2 years, or DES placement within the previous year, or if they underwent primary percutaneous coronary intervention (PCI) for acute ST elevation myocardial infarction (MI) or had treatment of the left main artery. Patients taking oral anticoagulation therapy and those who had contraindications to study drugs were also excluded.

The primary end point was a composite of death, MI, emergency target vessel revascularization, stroke, or major bleeding (TIMI criteria) within 12 months. Secondary end points included the same composite at 24 and 36 months, the individual components, and the incidence of TIMI minor and minimal bleeding. The study was stopped prematurely due to slow recruitment.

All patients were tested for aspirin resistance; 137 patients determined to be aspirin-resistant were not randomized. After 6 months of DAPT, patients who had no outcome-related events were randomized. A total of 1850 patients were randomized (n = 926 to 6 months of DAPT and n = 924 to 24 months of DAPT). Patient and procedural characteristics at baseline were similar between the 2 treatment arms. The study schematic and patient flow are illustrated in Figure 1.

The mean age of the population was 62 years, 80% were men, and the mean body mass index was 27 kg/m^2. Approximately 37% had type 2 diabetes, 15% had a previous MI, 23% had a previous PCI, and 5.8% had a previous coronary artery bypass graft. The PCI was considered a procedural success in > 98% of the patients randomized. Approximately 30% of patients had 2 lesions treated, and approximately 19% had ≥ 3 lesions treated. The majority of patients (> 98%) took clopidogrel.

There were no significant differences between the 2 arms at 12 months (Table 1). The noninferiority criteria were met between the 6-month and the 24-month DAPT groups (absolute risk difference, 0.11%; 95% CI, –1.04 to 1.26; $P_{\text{Noninferiority}} = .0002$).

To conclude, Prof Gilard noted several limitations of this trial. The study had a small sample size due to its premature discontinuation; however, because we finally had a rate of events of 1.5% (compared to 3% expected), we might consider that the sample size would be enough to consider the conclusion as valid, also because we are far from the boundary.

Table 1. ITALIC/ITALICplus Study Results at 12 Months (Intent-to-Treat Population)

End Point	24-Mo Group, No. (%) (n = 910)	6-Mo Group, No. (%) (n = 912)	HR (95% CI)	*P* Value
Primary				
Death from any cause, MI, stroke, TVR, or major bleeding	14 (1.5)	15 (1.6)	1.072 (0.517 to 2.221)	.85
Secondary				
Minor bleeding	4 (0.4)	5 (0.5)	1.247 (0.335 to 4.643)	.74
Minimal bleeding	6 (0.7)	6 (0.7)	0.997 (0.321 to 3.090)	.99
Death				
All deaths	7 (0.8)	8 (0.9)	1.143 (0.414 to 3.152)	.80
Cardiac death	3 (0.3)	5 (0.5)	1.667 (0.398 to 6.974)	.48
MI	4 (0.4)	6 (0.7)	1.500 (0.423 to 5.317)	.53
Stroke	4 (0.4)	0	NA	
TVR	2 (0.2)	5 (0.5)	2.499 (0.485 to 12.882)	.27
Stent thrombosis	0	3 (0.3)	NA	
Major bleeding	3 (0.3)	0	NA	

ITALIC/ITALICplus, Is There a Life for Drug Eluting Stent (DES) After Discontinuation of Clopidogrel; MI, myocardial infarction; NA, not applicable; TVR, target vessel revascularization.

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