heparins, and intravenous cangrelor, but success has been limited. Cilostazol, a phosphodiesterase inhibitor–type 3 that reversibly inhibits platelet activation and aggregation has shown promise as a third antiplatelet agent for high-risk patients and, given its shorter half-life, may be a consideration for perioperative bridging.

The OUTSIDE START Cilostazol Bridge Study, presented by Charles L. Laham, MD, Holy Family Memorial Hospital, Manitowoc, Wisconsin, USA, was a retrospective analysis conducted in patients who required surgery during the first 6 to 12 months after PES placement and discontinued DAPT. The analysis included consecutive patients who were bridged with cilostazol from 2 weeks to 60 months after a PES placement over an 8-year period.

The patients stopped DAPT 8 days before surgery and started cilostazol 100 mg BID on the seventh day preoperatively. Two dosing regimens of cilostazol 1300 mg were used to reduce the risk and degree of perioperative bleeding. Patients undergoing surgery with a low to moderate risk of bleeding had a goal of cilostazol 1300 mg, which they discontinued 24 to 30 hours before surgery. DAPT was resumed 12 to 24 hours after surgery. The goal for patients undergoing high-bleeding-risk surgery was cilostazol 1000 mg, which they stopped 54 to 60 hours prior to surgery. They restarted DAPT 24 to 36 hours after surgery. The primary end points were perioperative bleeding and MACE (cardiac death, myocardial infarction, or urgent revascularization) within the bridged period and up to 1 month after surgery.

A total of 108 patients with ≥1 PES who underwent 183 consecutive surgeries stopped DAPT and were bridged by cilostazol (Table 1). Of these, 104 (57%) surgeries were bridged with cilostazol 1300 mg, 60 (32%) with cilostazol 1000 mg, and 10 (5.5%) with 650 to 900 mg. A total of 171 surgeries were adequately bridged with >600 mg of cilostazol. The remaining 12 patients received an inadequate preoperative dose of 0 to 600 mg cilostazol and failed to resume DAPT postoperatively. No MACE occurred among patients who were successfully bridged with cilostazol. Among patients who were not adequately bridged perioperatively, 1 MACE occurred in the first year, and of note, 3 occurred beyond 12 months, of which 1 occurred up to 40 months post-PES stent placement. The study results are shown in Table 1.

Perioperative cilostazol for DES bridging is feasible in patients at the highest risk of stent thrombosis with PES and completely off DAPT. No MACE or bleeding other than minor nuisance bleeding was reported in patients who were successfully bridged with cilostazol. Dr Laham concluded that this was a clinically driven hypothesis-generating feasibility study. The results should be verified in controlled trials using current-generation DES and bare metal stents with antiplatelet agents in current use.

Table 1. OUTSIDE START Cilostazol Bridge Study: 8-Year Results, No. (%)

Timing of Surgical Bridging[a]	Adequate Bridging/DAPT Resumption	Suboptimal or No Cilostazol Bridge and/or Failed DAPT Resumption (Controls)	
	No MACE	No MACE	MACE[b]
<6 (26)	23 (88)	3 (12)	—
6-12 (29)	25 (86)	3 (10)	1 (3.4)[c]
>12-24 (49)	48 (98)	—	1 (2.0)[d]
>24-36 (48)	45 (94)	2 (4.2)	1 (2.1)[e]
>36-60 (31)	30 (97)	—	1 (2.9)[f]
Total (183)	171 (93)	8 (4.4)	4 (2.2)

Data presented in No. (%) unless otherwise indicated.

DAPT, dual antiplatelet therapy; MACE, major adverse cardiac event; PCI, percutaneous coronary intervention; PES, paclitaxel-eluting stent.

[a]Months post-PES (No. of bridged).

[b]Actual MACE by type and timing post-PES placement (events occurred only in those without adequate bridging).

[c]Urgent repeat PCI at 7.5 months.

[d]Death at 12.5 months.

[e]Urgent repeat PCI at 28 months.

[f]Myocardial infarction at 40 months.

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TRIAGE: Similar Ischemic and Bleeding Outcomes With Prasugrel and Clopidogrel

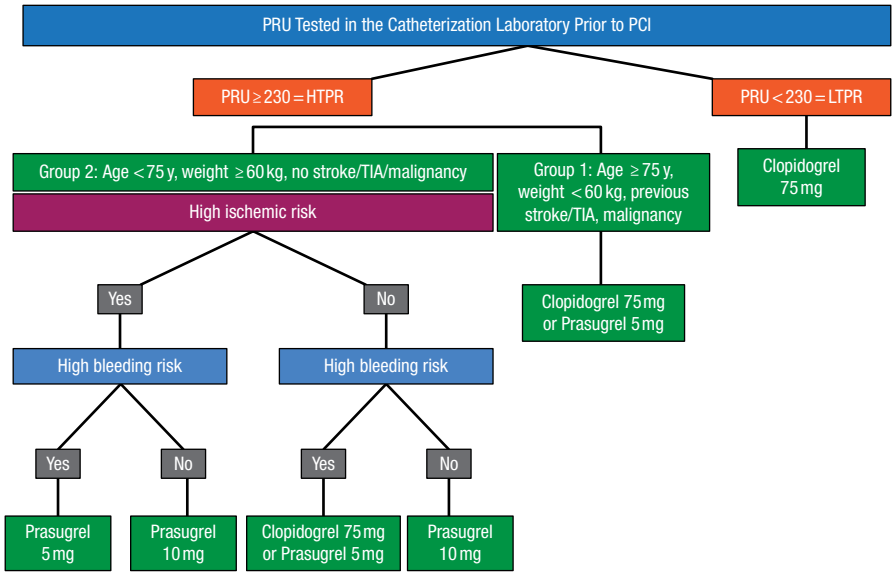
Written by Alla Zarifyan

Jaya Chandrasekhar, MBBS, Icahn School of Medicine at Mount Sinai, New York, New York, USA, presented results of the TRIAGE study [NCT01582217], demonstrating that patients with high on-treatment platelet reactivity (HTPR) receiving prasugrel and patients with low on-treatment platelet reactivity (LTPR) treated with clopidogrel had similar ischemic and bleeding outcomes.

HTPR in patients treated with clopidogrel is associated with a greater incidence of adverse cardiac events such as stent thrombosis, myocardial infarction (MI), and even death. However, testing platelet function prior to thienopyridine selection in patients undergoing percutaneous coronary intervention (PCI) has not been shown to correlate with improved outcomes in recent randomized trials, and the role of screening for platelet function in the context of ischemic and bleeding risks has not been investigated.

TRIAGE was a multicenter, prospective, observational study. The objective was to compare outcomes in patients treated with prasugrel vs clopidogrel at PCI

Figure 1. TRIAGE Study Algorithm



HTPR, high on-treatment platelet reactivity; LTPR, low on-treatment platelet reactivity; PCI, percutaneous coronary intervention; PRU, P2Y12 Reaction Units; TIA, transient ischemic attack. Reproduced with permission from J Chandrasekhar, MBBS.

following determination of platelet reactivity in conjunction with clinical risks. The primary safety and efficacy end points were the rate of major adverse cardiac events (MACE) and the rate of BARC type 2, 3, or 5 bleeding, respectively, at 1-year follow-up.

Platelet reactivity was tested immediately prior to PCI, and HTPR was defined as P2Y12 Reaction Units (PRU) ≥230. Patients were further split into treatment groups based on their ischemic and bleeding risk levels (Figure 1). High ischemic risk was defined as undergoing PCI for acute coronary syndromes or stent thrombosis, high angiographic risk PCI, or 30-day stent thrombosis score of ≥6. High bleeding risk was defined as having a bleeding risk score ≥10, recent surgery, recent bleeding history, or bleeding diathesis.

The anticipated study sample size was 1000 patients, but recruitment was terminated due to slow enrollment at 318 patients (mean age, 65.9 years; 19.0% women). Based on the study criteria, 40% of patients were classified to be at high ischemic risk, 58% with PRU ≥ 230 and/or high ischemic risk, and 34% at high bleeding risk. Clopidogrel was continued in 72% of patients, whereas 28% received prasugrel.

The primary efficacy end point did not differ significantly between treatment groups: MACE (death, nonfatal MI, or stent thrombosis) occurred in 3.5% of patients on clopidogrel and 4.4% on prasugrel ($P = .70$). The rate of secondary ischemic end points including periprocedural MI was also similar between the treatment groups with nonsignificant P values. The primary safety end point occurred in 7.9% of patients on clopidogrel and 5.6% on prasugrel ($P = .47$). The secondary bleeding end points were also nonsignificant, with patients on clopidogrel experiencing a numerically but not statistically higher rate of bleeding events.

MACE and secondary ischemic end points occurred at a similar rate in patients with PRU <230 and those with PRU ≥230. Analogously, when patients with PRU <208 were compared with those with PRU ≥208, ischemic end points were numerically but nonsignificantly different ($P = .08$).

In conclusion, the TRIAGE study did not find a significant difference between groups for any of the prespecified efficacy or safety end points. The low enrollment resulted in a sample size that was too small to detect any significant differences between groups. Other study limitations were the unblinded treatment, low event rate, and use of an unvalidated treatment algorithm, although it incorporated validated ischemic and bleeding score components. The difference in the number of ischemic and bleeding events between groups may suggest that platelet function testing may identify more patients at a high ischemic risk than clinical assessment alone, but this must be tested in a larger study.