Letter to the Editor

Effect of genotype-guided strategy in East Asian *vs.* Caucasian patients after percutaneous coronary intervention: insight from the TAILOR-PCI trial

Hyun Kuk Kim[1], Dirk Sibbing[2,3], Young-Hoon Jeong[4]

[1]Department of Internal Medicine, Chosun University College of Medicine, Gwangju, South Korea; [2]Department of Cardiology, LMU München, Munich, Germany; [3]DZHK (German Centre for Cardiovascular Research), partner site Munich Heart Alliance, Munich, Germany; [4]Department of Internal Medicine, Gyeongsang National University School of Medicine and Cardiovascular Center, Gyeongsang National University Changwon Hospital, Changwon, South Korea

Correspondence to: Young-Hoon Jeong, MD, PhD. Cardiovascular Center, Gyeongsang National University Changwon Hospital, 11 Samjeongja-ro, Seongsan-gu, Changwon, Gyeongsangnam-do, 51472 South Korea. Email: goodoctor@naver.com.

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In patients undergoing percutaneous coronary intervention (PCI), dual antiplatelet therapy (DAPT) with aspirin and $P2Y_{12}$ receptor inhibitor is the standard treatment to prevent occurrence of atherothrombotic event. Clinical application of different $P2Y_{12}$ receptor inhibitors (clopidogrel, prasugrel or ticagrelor) with varying levels of antiplatelet potency has enabled physicians to consider individualized treatment strategies, which may include escalation or de-escalation of $P2Y_{12}$ receptor inhibitor (1). A tailored DAPT approach may be possibly guided by platelet function testing (PFT) or genetic testing (2). The data of the TAILOR-PCI (Tailored Antiplatelet Therapy Following PCI) trial evaluated clinical efficacy and safety of genotype-guided strategy (potent $P2Y_{12}$ receptor inhibitor in cases with CYP2C19 loss-of-function allele) *vs.* conventional treatment with clopidogrel (3), which could be another important evidence showing inter-racial differences of clinical benefit according to the selected treatment method (including 38.3% of East Asians and 49.1% of the Whites). During antithrombotic treatment, East Asians *vs.* Caucasian patients have shown a reduced benefit for ischemic events, an increased hazard for bleeding events, and race-specific response for the antithrombotic drugs, which has been a well-described and clinically important phenomenon termed the "East Asian Paradox" (4-7).

To mention at the first place, there are different frequencies of gene polymorphisms contributing to effects of antithrombotic agents across races (8) (*Table 1*). In the TAILOR-PCI trial, East Asian cohort showed a higher frequency of the CYP2C19 loss-of-function allele carriage compared with the Caucasian cohort (59.2% *vs.* 25.8%, P<0.001) (3), which may indicate decreased effect of clopidogrel in East Asian population. Second, there have been different risks of ischemic event and unique clinical benefit achieved by an antiplatelet treatment according to race (9,10). In the TAILOR-PCI trial, despite the same treatment with clopidogrel in patients carrying the CYP2C19 loss-of-function allele, Caucasian patients showed increased risk of ischemic event by about 1.8-fold than Asian patients (7.3% *vs.* 4.1%) (3). In addition, the genotype-guided strategy *vs.* conventional treatment reduced the risk of 1-year ischemic event after index PCI by 1.4% (2.7% *vs.* 4.1%) and 2.6% (4.7% *vs.* 7.3%) in the Asians and Caucasians, respectively (3). Finally, response to antithrombotic agents and prevalence of adverse side effects related with these agents can be different between races (1-4,11-13). The exposures of ticagrelor and its major active metabolite (AR-C124910XX) are approximately 40% higher in East Asian individuals than in White individuals (4-7), which correlates with the level of platelet inhibition. During standard-dose ticagrelor treatment, East Asian patients have shown increased risks of clinically serious bleeding (about 2-fold risk of clinically serious bleeding *vs.* clopidogrel) (11,12) and discontinuation (e.g., 1-year discontinuation rate of ticagrelor and clopidogrel: 51.5% and 9.0% in the Korean National Health Insurance Service data) (13). In

Table 1 Clinical evidences from the TAILOR-PCI trial (3) and proposed treatment strategy

	East Asian patients	Caucasian patients
Prevalence of *CYP2C19* loss-of-function allele(s)	59.2%	25.8%
Ischemic event on genotype-guided *vs*. conventional strategy	2.7% *vs.* 4.1% (↓1.4%)	4.7% *vs.* 7.3% (↓↓2.6%)
Major bleeding on genotype-guided *vs*. conventional strategy	↑↑	↑
Proposed treatment strategy	Ticagrelor monotherapy after short-term DAPT with reduced-dose ticagrelor	TAILOR-PCI strategy

↑ increase, ↑↑ marked increase. DAPT, dual antiplatelet therapy; TAILOR-PCI, Tailored Antiplatelet Therapy Following PCI.

the TAILOR-PCI trial (3), 1-year discontinuation rate was higher during ticagrelor *vs.* clopidogrel treatment (32% *vs.* 11%, P<0.001), which might affect clinical efficacy and safety of the genotype-guided therapy.

Taken together, the relatively high participation rate of East Asian patients in the TAILOR-PCI trial may influence the results of the study, and the delicate comparative analysis may give a deep insight into inter-racial difference in clinical benefit of the genotype-guided strategy. Furthermore, further large-scale clinical trials examining race-based clinical outcomes for a specific antithrombotic strategy are warranted for reliably assessing clinical implications and possible advantages of a tailored treatment based on patient's race. Recent evidences suggest that ticagrelor monotherapy after short-term DAPT [from TICO (Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus Stent for Acute Coronary Syndrome) trial] (14) or a reduced-dose ticagrelor treatment (from expert consensus) (7,15) would be a better choice in East Asian population with acute coronary syndrome (*Table 1*).

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Footnote

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