



## Reply



Dear Editor,

We sincerely appreciate the comment by Lombardi et al<sup>1</sup> on our published paper.<sup>2</sup> Table 1 demonstrates the incidence of dyspnea and the discontinuation of ticagrelor due to dyspnea in

## Conflicts of interest

I.-C.C. and C.-H.L. have been on the speakers' bureau for AstraZeneca and Sanofi. T.-H.C. has been on the speakers' bureau for AstraZeneca and Sanofi, and ever received travel

Table 1  
Reported incidence of dyspnea and discontinuation of ticagrelor due to dyspnea in the literature.

Authors or acronym of the trial/year of publication	Study design	Study population	Patient number	Duration of follow-up (d or mo)	Incidence of dyspnea, n (%)	Discontinuation of the study drug in patients with dyspnea, n (%)
PLATO <sup>3</sup> /2009	RCT	ACS	T = 9333; C = 9291	12 mo	T = 1270 (13.8); C = 721 (7.8)	T = 79 (6.2); C = 13 (1.8)
ESTATE <sup>2</sup> /2016	Retrospective	ACS	T = 224; C = 224	164.3 ± 116.4 d	T = 47 (21); C = 26 (11.6)	T = 8 (17); C = 1 (3.8)
Subiakto et al <sup>4</sup> /2015	Retrospective	PCI for ACS	T = 100	30 d	T = 9 (9)	T = 9 (100)
Dehghani et al <sup>5</sup> /2014	Registry	ACS	T = 227	157.4 ± 111.7 d	T = 47 (20.7)	T = 7 (14.9)
Gaubert et al <sup>6</sup> /2014	Registry	ACS	T = 164	1 mo	T = 37 (22.6)	T = 15 (40.5)
Sánchez-Galian et al <sup>7</sup> /2015	Retrospective	ACS	T = 111	3 mo	T = 15 (14)	T = 2 (13.3)

Values are expressed as the mean ± SD, n (%), or median (interquartile range) where appropriate.

ACS = acute coronary syndrome; C = clopidogrel; ESTATE = the Study of The Efficacy and Safety of Ticagrelor versus clopidogrel in Acute coronary syndrome in Taiwanese; PCI = percutaneous coronary intervention; PLATO = the Study of Platelet Inhibition and Patient Outcomes trial; RCT = randomized controlled trial; T = ticagrelor.

patients who reported dyspnea in Phase 3/4 clinical trials<sup>3–7</sup> of acute coronary syndrome with available relevant data. Our study revealed that the incidence of dyspnea-related discontinuation of P<sub>2</sub>Y<sub>12</sub> antagonist treatment in patients with dyspnea tended to be higher in the ticagrelor group (17.0%),<sup>2</sup> which was similar to previous real-world studies.<sup>5–7</sup> When compared with clopidogrel treatment, ticagrelor causes a fourfold increase in the incidence of dyspnea requiring discontinuation of a P<sub>2</sub>Y<sub>12</sub> antagonist, according to our study<sup>2</sup>; the result was very similar to that of the Study of Platelet Inhibition and Patient Outcomes trial (a 3.4-fold increase).<sup>3</sup> In light of the advantages and disadvantages of randomized controlled trials and observational studies,<sup>8,9</sup> both clinical and observational evidence should not be mutually exclusive and should actually be complementary.

expenses and others, which are unrelated to research, to attend Annual Scientific Meetings of the European Society of Cardiology from AstraZeneca and Sanofi. Y.-H.L. has been on the speakers' bureau for AstraZeneca and Sanofi and ever received travel expenses and others, which are unrelated to research, to attend Annual Scientific Meetings of the American College of Cardiology from AstraZeneca.

## References

- Lombardi N, Crescioli G, Lucenteforte E, Mugelli A, Vannacci A. Ticagrelor safety profile in real-life setting of acute coronary syndrome patients. *J Chin Med Assoc* 2017;**80**:183–4.

DOI of Original article: <http://dx.doi.org/10.1016/j.jcma.2016.02.010>.

<http://dx.doi.org/10.1016/j.jcma.2016.11.004>

1726-4901/Copyright © 2017, the Chinese Medical Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

2. Chen IC, Lee CH, Fang CC, Chao TH, Cheng CL, Chen Y, et al. Efficacy and safety of ticagrelor versus clopidogrel in acute coronary syndrome in Taiwan: a multicenter retrospective pilot study. *J Chin Med Assoc* 2016;**79**:521–30.
3. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2009;**361**:1045–57.
4. Subiakto I, AsrarulHaq M, Van Gaal WJ. Bleeding risk and incidence in real world percutaneous coronary intervention patients with ticagrelor. *Heart Lung Circ* 2015;**24**:404–6.
5. Dehghani P, Chopra V, Bell A, Kelly S, Zulyniak L, Booker J, et al. Southern Saskatchewan ticagrelor registry experience. *Patient Prefer Adherence* 2014;**8**:1427–35.
6. Gaubert M, Laine M, Richard T, Fournier N, Gramond C, Bessereau J, et al. Effect of ticagrelor-related dyspnea on compliance with therapy in acute coronary syndrome patients. *Int J Cardiol* 2014;**173**:120–1.
7. Sánchez-Galian MJ, Flores-Blanco PJ, López-Cuenca A, Gómez-Molina M, Guerrero-Pérez E, Cambronero-Sánchez F, et al. Ticagrelor related dyspnea in patients with acute coronary syndromes: incidence and implication on ticagrelor withdrawn. *Int J Cardiol* 2015;**187**:517–8.
8. Nallamothu BK, Hayward RA, Bates ER. Beyond the randomized clinical trial: the role of effectiveness studies in evaluating cardiovascular therapies. *Circulation* 2008;**118**:1294–303.
9. Lombardi N, Crescioli G, Mugelli A, Vannacci A. Ticagrelor recommended over clopidogrel, only in clinical trials or also in a real-world practice? *Expert Rev Cardiovasc Ther* 2016;**14**:1103–4.

I-Chih Chen

*Division of Cardiology, Department of Internal Medicine,  
Tainan Municipal Hospital, Tainan, Taiwan, ROC*

Cheng-Han Lee

*Division of Cardiology, Department of Internal Medicine,  
National Cheng Kung University College of Medicine and  
Hospital, Tainan, Taiwan, ROC  
Institute of Clinical Pharmacy and Pharmaceutical Sciences,  
College of Medicine, National Cheng Kung University, Tainan,  
Taiwan, ROC*

Yi-Heng Li

Ting-Hsing Chao\*

*Division of Cardiology, Department of Internal Medicine,  
National Cheng Kung University College of Medicine and  
Hospital, Tainan, Taiwan, ROC*

\*Corresponding author. Dr. Ting-Hsing Chao, Division of  
Cardiology, Department of Internal Medicine, National Cheng  
Kung University College of Medicine and Hospital, 138,  
Sheng-Li Road, Tainan 704, Taiwan, ROC.  
*E-mail addresses: chaoth@mail.ncku.edu.tw,  
chaotinghsing@gmail.com, chaotinghsing@yahoo.com.tw  
(T.-H. Chao).*