Received: 22 September 2021 | Revised: 24 October 2021 | Accepted: 27 October 2021

DOI: 10.1002/rth2.12625

rpth research & practice in thrombosis & haemostasis

LETTER TO THE EDITOR

Safety of the second dose of the ChAdOx1 nCoV-19 vaccine in people with persistent anti–platelet factor 4 antibodies

Vaccine-induced immune thrombotic thrombocytopenia (VITT) typically occurs after the first dose of the ChAdOx1 nCoV-19 vaccine, while it is very rare after the second dose. The rate of thrombosis with thrombocytopenia after the second ChAdOx1 vaccination is within an estimated background range of an unvaccinated population.[1] However, safety data of the second dose of the ChAdOx1 vaccine in people with persistently positive anti–platelet factor 4 antibodies (anti-PF4 Abs) are still lacking. Whether a second dose of the ChAdOx1 vaccine would enhance anti-PF4 Ab production and activity leading to platelet consumption and coagulation activation remains unknown. We recently published a prevalence of 3.1% (16/521) nonpathogenic anti-PF4 Abs among Thais receiving the first dose of the ChAdOx1 vaccine.[2] Of those, we could obtain blood samples from 13 participants with persistently positive anti-PF4 Abs 8 to 10 weeks after first ChAdOx1 vaccination and were administered a second dose. We then monitored platelet counts, anti-PF4 Abs (Zymutest HIA IgG; Hyphen Biomed) and D-dimer levels (Biomerieux) 2 weeks after the second vaccination. Neither new onsets of thrombocytopenia nor elevated D-dimer levels were documented. There were no statistical differences using repeated measures analysis of variance of platelet counts and anti-PF4 Ab optical density (OD) values, while D-dimer levels were significantly decreased during a follow-up (Figure 1). Of note, a significantly elevated D-dimer level in only one participant after the first vaccination declined to normal after the second ChAdOx1 dose. D-dimer levels in other participants remained normal (<500 ng/mL) during the follow-up. Anti-PF4 Abs remained detectable (a cutoff OD value <0.25) in all 13 participants after second vaccination. None of the detectable anti-PF4 Abs activated platelets in light transmission aggregometry. All participants showed no symptoms and signs related to thrombosis up to 12 weeks, supporting their nonfunctionality.

This follow-up study suggests that a second dose of the ChAdOx1 vaccine neither increases anti-PF4 Ab generation nor alters anti-PF4 Ab functionality in people with preexisting nonpathogenic anti-PF4 Abs. Therefore, a second dose of the ChAdOx1 vaccine is safe to be administered to people with detectable nonfunctional anti-PF4 Abs after the first vaccination. Although our findings are limited by the small sample size and may need to be confirmed with a larger cohort, these preliminary data provide the first evidence to assure the safety of second ChAdOx1 vaccination in people with persistently positive nonfunctional anti-PF4 Abs.

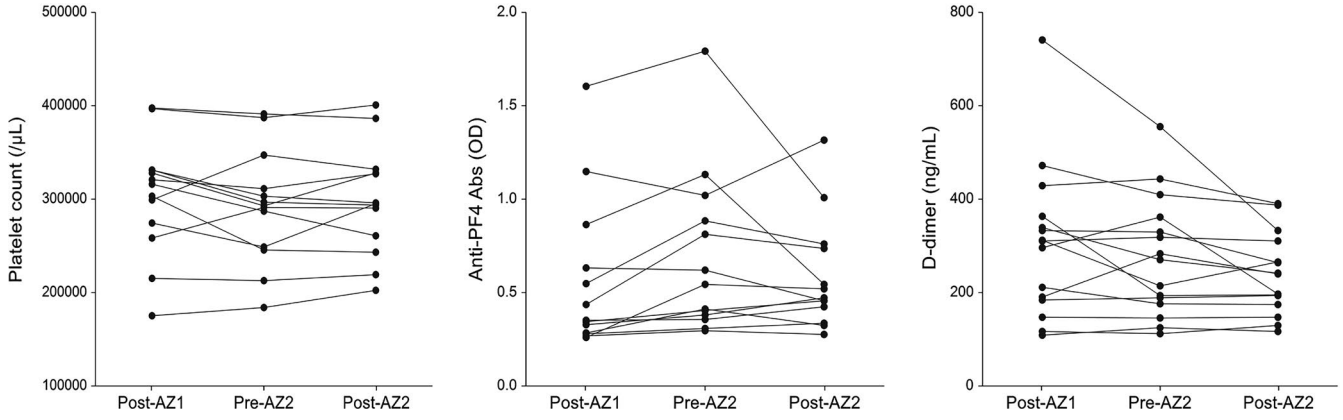

FIGURE 1 Platelet counts, anti–platelet factor 4 antibodies, and D-dimer levels in participants with persistent anti-PF4 antibodies and were administered a second dose of the ChAdOx1 nCoV-19 vaccine. There were no significant changes in platelet counts ($P = .35$) and anti-PF4 antibodies ($P = .16$) except a significant decline in D-dimer levels ($P = 0.03$). Post-AZ1, post first ChAdOx1 nCoV-19 vaccination; Pre-AZ2, prior second ChAdOx1 nCoV-19 vaccination; Post-AZ2, 2 weeks post second ChAdOx1 nCoV-19 vaccination

FUNDING INFORMATION

Thai Society of Hematology; Research Funding of Division of Hematology, Chulalongkorn University; Jaikrating Foundation; King Chulalongkorn Memorial Hospital

ACKNOWLEDGMENTS

This study was funded by a grant from Jaikrating Foundation; King Chulalongkorn Memorial Hospital; Research Funding of Division of Hematology, Chulalongkorn University; and Thai Society of Hematology.

RELATIONSHIP DISCLOSURE

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

AUTHOR CONTRIBUTIONS

NU, PW, LP, and PR designed the study. RV, ST, WJ, and TT collected data. BA, and AS performed laboratory tests. NU analyzed data and wrote the first draft of the manuscript. All authors discuss data, revised the manuscript, and approved the final version for publication.

Noppacharn Uaprasert MD[1,2]
Sasinipa Trithiphen MD[1]
Autcharaporn Sukperm BSc[1,2]
Benjaporn Akkawat BSc[1,2]
Phandee Watanaboonyongcharoen MD[3]
Rattaporn Vichitratchaneekorn MD[3]
Thanisa Tongbai MD[4]
Watsamon Jantarabenjakul MD, PhD[5]
Leilani Paitoonpong MD[6]
Ponlapat Rojnuckarin MD, PhD[1,2]

[1]*Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*
[2]*Research Unit in Translational Hematology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*
[3]*Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*
[4]*Department of Radiology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*
[5]*Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*
[6]*Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*

Handling Editor: Dr Cihan Ay.

Correspondence
Noppacharn Uaprasert, Division of Hematology, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital Rama IV Rd, Pathumwan, Bangkok 10330, Thailand.
Email: drnoppacharn@yahoo.com

ORCID

Noppacharn Uaprasert https://orcid.org/0000-0003-4562-9139
Ponlapat Rojnuckarin https://orcid.org/0000-0001-7912-1996

TWITTER

Noppacharn Uaprasert @noppacharn

REFERENCES

1. Bhuyan P, Medin J, da Silva HG, et al. Very rare thrombosis with thrombocytopenia after second AZD1222 dose: a global safety database analysis. *Lancet*. 2021;398:577-578.
2. Uaprasert N, Watanaboonyongcharoen P, Vichitratchaneekorn R, et al. Prevalence of thrombocytopenia, anti–platelet factor 4 antibodies and D-dimer elevation in Thai people after ChAdOx1 nCoV-19 vaccination. *Res Pract Thromb Haemost*. 2021;5:e12580.

How to cite this article: Uaprasert N, Trithiphen S, Sukperm A, et al. Safety of the second dose of the ChAdOx1 nCoV-19 vaccine in people with persistent anti–platelet factor 4 antibodies. *Res Pract Thromb Haemost*. 2021;5:e12625. doi:10.1002/rth2.12625