JACC: HEART FAILURE VOL. 4, NO. 6, 2016
JUNE 2016:516–20

4. Lee MS, Eum KD, Rodrigues EG, et al. Effects of personal exposure to ambient fine particulate matter on acute change in nocturnal heart rate variability in subjects without overt heart disease. Am J Cardiol 2016;117:151–6.

5. Langrish JP, Mills NL, Chan JK, et al. Beneficial cardiovascular effects of reducing exposure to particulate air pollution with a simple facemask. Part Fibre Toxicol 2009;6:8.

Antibody-Based Protection of von Willebrand Factor Degradation

Recently, Bartoli et al. (1) reported on the use of doxycycline to reduce ADAMTS-13-mediated von Willebrand factor degradation during supraphysiological shear stress. We have read their article with interest, noticing reference in their discussion to one of our recent publications that appeared in *Thrombosis and Haemostasis* (2). However, we would like to correct some significant misinterpretations of our data as cited by the investigators. Indeed, our antibody is referred to as a monoclonal antihuman ADAMTS-13 antibody. This is incorrect. In fact, we have reported on the discovery and characterization of a monoclonal antihuman von Willebrand factor antibody, designated Mab508. This is not only clearly written in the abstract, but our article also describes in detail the epitope within von Willebrand factor that is recognized by this antibody. Describing our antibody as being antihuman ADAMTS-13 is therefore an important oversight.

Second, the investigators suggest that our antibody blocks ADAMTS-13 activity by 83% and that such widespread inhibition may inadvertently provoke a hypercoagulable, thrombotic thrombocytopenic purpura-like state and thrombosis. The investigators seem to confuse 2 types of experiments reported in our article. First, we clearly show that the anti-von Willebrand factor antibody blocks binding and degradation of von Willebrand factor by ADAMTS-13 by a maximum of 50%. The figure 83% actually refers to the inhibition of the high-molecular weight multimers, not of von Willebrand factor as a whole. This is an essential difference, as it actually prevents (rather than induces) Mab508 from provoking the occurrence of ultralarge von Willebrand factor multimers that could potentially induce thrombotic thrombocytopenic purpura-like symptoms. This specificity is an important strength of our antibody, particularly when compared with the nonspecific inhibition of ADAMTS-13 and other proteases that is achieved when using doxycycline.

We hope that this letter clarifies the scope of our article (identification of an anti-Von Willebrand factor antibody that partially interferes with ADAMTS-13-mediated degradation).

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Please note: Drs. Lenting, Denis, and Susen are inventors on a patent related to Mab508 that is owned by Inserm-Transfert SA. Dr. van Belle has reported that he has no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Bartoli CR, Kang J, Restle DJ, et al. Inhibition of ADAMTS-13 by doxycycline reduces von Willebrand factor degradation during supraphysiological shear stress: therapeutic implications for left ventricular assist device-associated bleeding. J Am Coll Cardiol HF 2015;3:860–9.

2. Rauch A, Legendre P, Christophe ODF, et al. Antibody-based prevention of von Willebrand factor degradation mediated by circulatory assist devices. Thromb Haemost 2014;112:1014–23.

REPLY: Antibody-Based Protection of von Willebrand Factor Degradation

Thank you for the opportunity to respond to Dr. Lenting and colleagues. In our paper that examined doxycycline to reduce ADAMTS-13-mediated von Willebrand factor (vWF) degradation during left ventricular assist device (LVAD)-like shear stress (1), we referenced a recent paper by Rauch et al. (2).

In their study, Rauch et al. (2) used a monoclonal antibody (mAb508) to block ADAMTS-13/vWF interactions in order to preserve high-molecular-weight vWF multimers. We acknowledge that “anti-ADAMTS-13” antibody was incorrect terminology and that their antibody is in fact an anti-vWF antibody that blocks the ADAMTS-13/vWF interaction. We congratulate Dr. Lenting and colleagues for this important mechanistic work with potential therapeutic implications. However, we disagree with statements made in their recent Letter to the Editor. Other than correcting the terminology, our concern that mAb508 therapy may lead to hypercoagulability and thrombosis remains unchanged.