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Thrombocytopenia with acute ischemic stroke and bleeding in a patient newly vaccinated with an adenoviral vector-based COVID-19 vaccine: COMMENT from Gruel et al.: RESPONSE from Kahn et al.

We acknowledge the commentary of Gruel et al. on our recent letter¹ and are pleased that the authors agree that IdeS (Imlifidase) may be a potential treatment option for the rare but potentially severe IgG-mediated platelet activation observed in complications to vaccination with ChAdOx1 nCoV-19. It is apparent that our respective but distinct expertise regarding IdeS has led us to develop this hypothesis in parallel. As we clearly cited in our original letter these authors have previously contributed important evidence that IdeS may be beneficial in treating IgG-mediated platelet dysfunction in a mouse model of heparin-induced thrombocytopenia.² The intention with our letter was to provide more background to IdeS and insight into the unique properties of IdeS that make it suitable for treating many manifestations of IgG-mediated human disease.

In a series of publications following our discovery of IdeS in 2001,³ we described the specific, complete, and rapid cleavage of human IgG *in vitro* and *in vivo* by IdeS, and also the dramatic effect of the enzyme on autoimmune conditions, including a mouse model of IgG-mediated thrombocytopenia.⁴ The finding that IdeS also cleaves anti-platelet factor 4 IgG antibodies is therefore entirely expected. However, the recent publications on this topic are not focused on the opportunity of IdeS treatment in patients with an acute thrombosis with thrombocytopenia syndrome post-vaccination with ChAdOx1 nCoV-19. Therefore, in our letter we wanted to present some background to this unique and fascinating enzyme and its clinical potential to hematologists investigating this novel syndrome. Moreover, because IdeS (Ideferix) was recently approved as a drug within the EU, much due to our work for 20 years, we found it particularly important to spread this information to physicians treating these severely ill patients.

KEYWORDS

drug-related side effects and adverse reactions, IdeS, platelet factor 4, thrombocytopenia, vaccine

CONFLICTS OF INTEREST

Dr. Kahn and Prof. Björck have stock ownership in Hansa Biopharma. Prof. Björck is listed as inventor on two patents for IdeS owned by

Hansa Biopharma AB. Prof. Björck has received grants from Hansa Biopharma until the end of 2020.

AUTHOR CONTRIBUTIONS

The authors have drafted and written the manuscript together.

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