Authors’ Reply: Anti-Hinge Antibodies Are Likely to Be of Minor Importance

First, we would like to thank Borza and Manral for their interest in our study GOOD-IDES-01. In this study, 15 patients with anti-glomerular basement membrane antibodies and an eGFR <15 ml/min were given a single dose of 0.25 mg/kg imlifidase on top of standard of care. This led to a rapid decline of circulating autoantibodies and, at 6 months, ten patients were alive with functioning native kidneys. In their letter, Borza and Manral suggest the reason why more patients did not have their kidney function salvaged could be due to anti-hinge antibodies preferentially reacting with neoepitopes formed after IgG cleavage with imlifidase.

When trying to perform a post hoc analysis of the treatment failures, it is important to know that one more patient was able to stop dialysis after the end of the study, at 8 months after imlifidase treatment. Thus, at 1 year, 73% of patients were alive and free of dialysis. There are several possible reasons why not all of the patients responded to treatment, including severity of damage at the start of treatment, tubulointerstitial fibrosis, other pathogenic mechanisms (i.e., T cells, anti–neutrophil cytoplasm antibodies), magnitude of autoantibody rebound, epitope specificity of the autoantibodies at rebound, and anti-hinge antibodies.

The significance of anti-hinge antibodies has been discussed in the literature (as referenced by Borza and Manral) and, although these antibodies can be detected in vivo and have the ability to restore the Fc-function of fragmented antibodies in vitro, the effect of anti-hinge antibodies after imlifidase treatment is likely NS during the early course after treatment because the levels are low, they are cleaved by imlifidase on top of functioning native kidneys. In their letter, Borza and Manral suggest the reason why not all of the patients responded to treatment and at rebound, but we are inclined to be more concerned over rebound of anti-glomerular basement membrane antibodies.

DISCLOSURES

C. Kjellman reports being employed by, having ownership interest in, and having patents or royalties with Hansa Biopharma AB. M. Segelmark reports having consultancy agreements with AstraZeneca, Hansa Biopharma AB, Toleranzia AB, and Vifor Pharma; receiving research funding from Hansa Biopharma AB; and spouse being employed by Nanoecho AB Sweden.

FUNDING

None.

AUTHOR CONTRIBUTIONS

C. Kjellman and M. Segelmark reviewed and edited the manuscript; and M. Segelmark conceptualized the letter, wrote the original draft.

REFERENCES


Mårten Segelmark and Christian Kjellman

1Department of Clinical Sciences, Lund University, Lund, Sweden
2Hansa Biopharma AB, Lund, Sweden

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Prof. Mårten Segelmark, Department of Clinical Sciences, Lund University, Lund, Skane, Barngatan 2, 22185 Lund, Sweden. Email: marten.segelmark@med.lu.se

Copyright © 2022 by the American Society of Nephrology

JASN 33: xxxxxx, 2022

ISSN : 1533-3450/1046-xxxx

1