Peer Review File

Article information: https://dx.doi.org/10.21037/aob-23-46

Reviewer Comments

Reviewer A

Comment 1: Line 206: Was [24; 1998] the first report of anti-ADAMTS13 antibody? If so, this should be stated.

Reply 1: The suggested change to include a reference to the first report of an anti-VWF-cp inhibitor was incorporated into the manuscript.

Comment 2: Line 266: Remove the word 'the' - it should read, "...realizations about blood and how it works."

Reply 2: The suggested change in wording was made and is now reflected in the resubmitted manuscript.

Reviewer B

Comment 1: It is not clear what criteria were used to select articles for review. The introduction and methods are written in the style of a scoping review, but the inclusion/exclusion criteria are not described. The article does not even follow the convention for a narrative review. Instead, this is written like an editorial. I would recommend rebranding as such.

Reply 1: We appreciate the reviewer's perspective on the nature of the manuscript as submitted. As outlined in the methods section, we did consider the inclusion of thousands of articles, but with the expertise of the two senior authors of this review, as well as the collective experience and knowledge base of all authors, only a select few references were highlighted, which was necessary not only to limit the scope of a broad and vast topic but also to avoid redundancy and hone the narrative of the review. Towards that end, the specific range and depth of the review were tailored as requested for this invited manuscript, which is part of a larger series of reviews about TTP. As such inclusion criteria and exclusion criteria are defined in the context of the discretion of the authors to tailor the narrative, which we believe is implied in the methods section as written as well as elsewhere in the manuscript.

Comment 2: The discussion of TTP is incomplete from a historical perspective, as the etiology of symptoms associated with TTP is not described. For example, TTP was once described as a pentad of symptoms, but this has fallen out of favor. The thresholds of diagnostic markers are not described, nor are the relationships to other MAHA's.

Reply 2: The authors appreciate the reviewer's comment on the diagnostic parameters that define the disease as well as the historic "pentad" of symptoms often associated with TTP. In the case of this review, we have chosen to focus on the pioneers of the field whose insights have led us to a more precise and functional definition of the disease, again highlighting that this review is not meant to be a comprehensive review

of every aspect of the history of the disease. Nonetheless, the reviewer's comments are appreciated and taken in the spirit in which they were written.

Comment 3: Recombinant ADAMTS13 therapy is not well described and should be included now that the drug is FDA-approved. The authors could discuss the significance of this in the context of the reviewed history and make the case for basic and clinical science coming together to solve important problems for patients.

Reply 3: We appreciate the reviewer's insights into the utilization of recombinant ADAMTS13 in a clinical context and how it relates to the past, particularly as the reviewer highlights how we have attempted to contextualize the current landscape of the treatment of the disease. As we have outlined in the "perspectives" section, we essentially agree with the reviewer and make the case that innovations in the field are only possible because of the hundreds, if not thousands, of scientists whose work has led us to this moment. As the reviewer notes, we did mention recombinant ADAMTS13 in the manuscript and believe that a more in-depth discussion of TTP treatment is better left for a different review, as this is outside the intended scope of this particular manuscript.