Reviewer’s report

Title: Vedolizumab Trough Level Monitoring In Inflammatory Bowel Disease: A State Of The Art Overview

Version: 0 Date: 01 Feb 2019

Reviewer: Joshua Korzenik

Reviewer’s report:

The authors address an interesting and important question in their commentary, if therapeutic drug monitoring (TDM) is beneficial in the use of vedolizumab. The manuscript presents a well written overview of current knowledge on the topic including real world data from post hoc analyses and observational series to support their position that an exposure-efficacy relationship (EER) exists with vedolizumab. Ward et al, recently published a review on the same topic. The authors conclude that the available data confirm EER of vedolizumab. However, the current body of evidence is not close to being definitive and offers several reasons to be more skeptical of the benefit of trough monitoring with vedolizumab than the authors suggest. I

The pharmacokinetic profile of vedo differs in many respects from anti-TNF therapy, where TDM has been demonstrated to deliver more clinically effective dosing. Additionally, while antibody development may increase clearance of vedolizumab, available data suggests that antibody development is a less common event in anti-integrin therapy compared to anti-TNF. Trough level alone may be inadequate to predict clinical response and may not yield much benefit over clinical judgment to guide therapeutic decisions. Furthermore, results from cross sectional studies should be interpreted with caution due to heterogeneous study designs, including varying definitions of response and remission. As a result, it is difficult to confirm causation from associations between drug level and reported clinical outcomes. As arguments on both sides are speculative and supported by limited data, additional skepticism might strengthen the article to express the idea that we cannot extrapolate from the anti-TNF data to assume that there will be a clear role for TDM in using vedo. In anti-TNF TDM, the utility has been strengthened by clinical concerns in a patient with secondary loss of response and whether the subsequent medication would best be another in the same class or a medication with a different mechanism. As there is not yet another medication in the same class as vedo and antibody development appears much less, the same utility with vedo is attenuated and the utility of TDM may be more marginal. The authors touch on this but might discuss in more detail. on-for loss of response vs pro-active, as is being debated in anti-TNF therapy.

The manuscript could also be improved if authors addressed the context of TDM in vedo. It is worth commenting on how to best incorporate TDM with vedolizumab (ie. primary versus secondary nonresponse or proactive versus reactive testing). Additionally, authors could have commented on the differences in reported trough effect between UC and CD that were described in the GEMINI 2 and 3 trials, where the effect was more modest in CD.
Lastly, although a minor issue, there are a couple typos as well as awkward phrases in the manuscript which can be improved upon.

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