Reviewer 1

1. "critical appraisal" is not correct, this is rather a review. To make this a critical appraisal, the authors need to evaluate the material in an interpretive fashion and not merely repeat what is written in the literature.

Accepted: Title changed

2. The first 3 paragraphs could be condensed.

Done: Condensed to two paragraphs

3. The essential question is: how many patients will fail current therapies and so become available for vedolizumab (VEDO) therapy?

Reply: Still unanswered question, so unable to comment further.

3 Is a detailed account of the mechanism of action of VEDO needed in what is essentially a clinical paper? This part could be shortened

Done: but clinicians should understand the science behind the drug.

The account of the various trials is comprehensive but difficult to follow. You could consider tabulating the essential data so make it more amenable to the understanding of the reader. In such a table you should explain the clinical scores in a footnote (such information is lacking in the manuscript). Furthermore, are the authors aware of new trials in progress? It is easy to access this from clinical trail registries. Such information will add more perspective.

Reply : Table 1,2 provided.

5 Again, consider expanding and tabulating the section on adverse effects

Done as above

6 There are other matters of interest, such as use in limited disease such as refractory proctitis, use in combination with other agents, the cost issues with this drug. How would the authors feel about prolonged use of VEDO, or VEDO with an immunosuppressant?

Reply: This is beyond the remit of a review.

Reviewer 2

1. Under the section on “Adverse Effects”, I think it is important to indicate how many patients in these trials responded to the antibody therapy by producing anti-antibody which would make them refractory for future therapy and also add to the data base as to the safety of the use of such antibody based therapies and if significant may require monitoring of the patients in future studies for the induction of such antibodies prior to repeated therapy with such an antibody formulation. Recognizing that the number maybe small, it is nonetheless important to document for the reader.

Reply: To my knowledge, the full data has still not been released.

2. In addition, I believe the paper by Wyant T et al (Gut 64:77, 2015) needs to be included because it addresses a very important issue with regards to the effects of Vedoluzimab on immune responses. Thus, the issue has always been raised whether the administration of the antibody is immunosuppressive or not. The findings clearly show that at the doses administered, while Vedoluzimab inhibits response to oral cholera vaccine (which it was supposed to do), it had no effect on hepatitis B vaccine responses suggesting differential effects on oral versus parenteral immunizations at least by limitations of a single dose administered and in an otherwise healthy population. 3. One of the issues that does not come clear from the paper is the role of the stage of the patient and their ability to responds to Vedoluzimab therapy. Is there a way to stratify the data and/or analyze the Phase I, II and III data and show whether the clinical stage and/or number of years post initial diagnosis plays a role in the response to Vedoluzimab?

Reply: No

4. For additional references, the author should include the review by Poulakos M et al, J Pharmacy Practice 1-13, 2015.

   Reply: Good paper, but we have referred to original sources.