

Dear Editors of *World Journal of Gastroenterology*,

We are pleased submitting back a new revised version of our opinion review article entitled “**Use of granulocyte/monocytapheresis in ulcerative colitis: A practical review from a European perspective**” with the number of reference 61586, for reconsideration and eventual publication in *World Journal of Gastroenterology* if we were able to adequately respond to the comments made by the editors.

We have read all the comments and suggestions and, accordingly, made the suggested changes which we are sure have improved the quality of our article. We hope that now it will be suitable for publication. In this document, we respond to all comments.

Thank you for receiving this new revised version of our manuscript.

Sincerely yours,

Eugeni Domènech, M.D., Ph.D.

Corresponding author

We thank all the editors and reviewers the comments and suggestions, which we have dealt with, as follows:

Reviewer #1:

The authors have reviewed some data on the use of GMA from Europe. The presentation needs to be more structured. It would be much informative to have a pros and cons segments in the article. There is no explanation on how they gathered the data.

The guidelines of the World Journal of Gastroenterology state that the "Opinion reviews" must be "focused on the status quo of the overall research in the field, highlighting the most important research topics, the problems that have now been resolved and remain to be resolved, and the future research directions that may maximize the practical impact on a field". No specific recommendations on the structure of the manuscript are given. In line with this, we decided to follow a manuscript structure according to our aims of giving "an overview of the mechanism of action, recent clinical data and practical aspects of GMA use in UC from a European perspective". Similarly, as the Opinion reviews are not systematic reviews and, according to the editorial guidelines, they have to highlight the most important research topics, we performed a literature search for "apheresis" and "ulcerative colitis" and chose those studies and articles that we thought were more relevant.

The issue of cost was not covered.

A comment on treatment economic burden has been included at the end of the "Role of GMA in UC management" section.

The reason for unpopularity in Europe and west as compared to Japan needs to be discussed.

We agree with the reviewer that this is an interesting issue. In spite of the lack of well-established arguments for this and that the initial controlled European trials of GMA in the early 2000s (in the pre-biologic era of UC) yielded promising results, the negative results of an American double-blind, sham-controlled RCT for moderate-to-severe active UC and the licensing of anti-TNF agent use for UC, led to a consequent loss of interest in GMA in Europe (as stated in the first paragraph of the "Role of GMA in the management of UC" of the manuscript). Beyond this, we are not aware of other clear arguments. In fact, the use of GMA is quite heterogenous throughout Europe, being part of the UC armamentarium in Scandinavia, Spain, Italy or Germany, and much less used in France, Portugal and Greece.

The title might be better to be changed to European experience rather than opinion.

The aim of this manuscript is to provide a practical overview by several European gastroenterologist experienced with the use of GMA in ulcerative colitis. However, the manuscript does not report our own experience but reflects the authors' opinion based on the available data, particularly those studies coming from European controlled studies. In fact, the title do not include the word "opinion" but "perspective", which we feel the most suitable in line with the goals of our manuscript.

Reviewer #2:

This manuscript is well written review showing recent advancement of GMA therapy in contrast with other IBD treatments. And this paper has successfully documented a certain new established academic process in Europe and in Japan. I think this paper is published as it is.

We thank the positive comments of the reviewer.

Editorial office's comments

Science editor: The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

We have provided the original picture in a PowerPoint file.