

Dear Reviewers, Thank you for giving me the opportunity to submit a revised draft of our manuscript. We have been able to incorporate changes to reflect most of the suggestions provided by the reviewers. We have highlighted the changes within the manuscript.

Reviewer 1

Comment: Overall the article lacks a main logistic flow. The title clearly state “nanomedicine”, but a considerable portion of the article describes immunotherapy and checkpoint blockade therapy, give an impression of lack of focus.

Author’s answer: Our review focuses on the application of nanoparticles in cancer treatment including immunomodulatory agents and immune checkpoint inhibitors. Since nanoparticles addresses the enhancement of the efficacy of these treatments by using nanoparticles as “vehicles” that contain the active molecules, we saw fit to explain the aim of these treatments.

Comment: The entire immune checkpoint inhibitor section appeared had no relevance with nonamedicine.

Author’s answer: The aim of that part was to describe the function of these inhibitors that will be boosted by nanomedicine. However, as kindly remarked, we added a section describing the use of nanocarriers to enhance the effects of checkpoint inhibitors.

Comment: The NK cell section included CAR-T therapy, which seems mixed content.

Author’s answer: A separate section was added to be more precise.

Comment: At least, the concept of nanomedicine needs a clear definition in the beginning. Introduction section, first paragraph, the last sentence, “ultimately hindering the cell cycle”, hindering cell cycle? Please explain.

Author’s answer: The concept of nanomedicine was defined more accurately, as kindly indicated. Regarding the last sentence, that section was rephrased for its meaning to be clearer.

Reviewer 2

The article is very interesting, but I have a few concerns 1.

Comment: The title should be specific for oncologic malignancies.

Author's answer: Thank you for your comment. Our title "Nanomedicine approaches for the treatment of hematologic and oncologic malignancies" was chosen to make clear that both solid and hematologic malignant tumors are mentioned.

Comment: It is better to mention separately pre-clinical evidence and clinical evidence for each type of formulation.

Author's answer: Tables 1 and 2 list the clinical trials that are ongoing or completed while in the text the words "clinical" or "pre-clinical" are used so as for the reader to comprehend whether clinical or preclinical data are described.

Comment: The abstract can be included with details of type of formulation mentioned in the content.

Author's answer: The abstract was updated as kindly indicated.

Comment: The graphical abstract will be helpful for understanding the content. Not found any details on liver cancer-based formulation in the table or content?

Author's Answer: We understand the benefits of a graphical abstract but unfortunately, but currently we are unable to create such a figure.

We look forward to hearing from you in due time regarding our submission and to respond to any further questions and comments you may have.

Sincerely

Maria Gazoulli