

16 February 2023

Respected Sir/Madam

Reference#: 81922

Title: Systemic treatment for metastatic colorectal cancer

I am hereby giving points response to your comments;

Reviewer #1

Comment #1: It is a well-written manuscript, in which the authors reviewed systemic treatment for metastatic colorectal cancer, including chemotherapy, targeted therapy, and immunotherapy. Minor suggestions as follows. 1. Add more figures to make the manuscript more attractive and illustrative. 2. Tables could be added to help the readers have a good knowledge of the latest progress in chemotherapy, targeted therapy, and immunotherapy.

Author answer: Thank you very much for your valuable comments and suggestions. I already added a figure to improve the quality of the manuscript. In addition, I included 1 table to summarize systemic treatment with targeted therapy and immunotherapy.

Reviewer #2

Comment #1: This article provides a systematic and detailed review of the treatment strategies and progress of mCRC, which is strongly supported by the results of many clinical trials and focuses on systemic treatment strategies for liver metastatic colorectal cancer. But there are a few caveats: 1. This paper focuses on treatment, but the charts in this paper are mainly about the risk factors and molecular mechanisms of mCRC. Is it possible to draw additional charts or tables to outline the treatment strategies mentioned in this paper? 2. The author mentioned the treatment for tumour microenvironment in the introduction, does it just mean immunotherapy? As far as I know, the immune system knowledge of tumour microenvironment is part of the tumour microenvironment, and there are other therapeutic modalities that may be affected by tumour microenvironment treatment of tumour, the author can appropriately add. In addition, does mCRC have other immunotherapeutic possibilities besides immune-checkpoint inhibitors and CAR T therapy (although it may not have been systematically validated in clinical trials)? 3. The author focuses on systemic treatment of liver metastatic colorectal cancer, but this is a direction of mCRC treatment. It may be more appropriate to discuss liver metastatic colorectal cancer after discussing the overall treatment of mCRC. At the same time, it is hoped that the author can discuss the treatment strategies especially for liver metastatic colorectal cancer in the conclusion. 4. The article is smooth in language, but contains some grammatical mistakes. For example, "harmatomatous" in "POLYPS" in "RISK FACTORS FOR COLORECTAL CANCER" seems to have a spelling mistake.

Author answer: Thank you very much for the important comments and advice. 1.) I already inserted a figure to improve understanding regarding the systemic treatment. 2.) I've already revisited the topic of tumour microenvironment and included a section of it in the manuscript. 3.) I have already made the changes you suggested to the manuscript. 4.) I have already corrected the errors.

Best regards,

W. Leowattana

Assoc.Prof.Dr.Wattana Leowattana

Tawitthep Leowattana

Dr.Tawithep Leowattana

Pathomthep Leowattana

Dr.Pathomthep Leowattana