

## Response to Reviewer's Comments

### Reviewer #1:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** The study systematically reviewed the evolutionary trends in the development of CRC treatments, and explored the potential of new therapies and how they might be used in combination with traditional therapies, as well as their advantages and disadvantages as future drugs. These summaries provided guidance for clinicians to learn and communicate.

### Reviewer #2:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** Very good work, the authors present many new promising therapeutic approaches, although still in the preclinical stage.

**All the responses has been marked in red colour**

**1 :** In the part of Radiation therapy, local radiotherapy can also be preoperatively downgraded, thereby increasing the rate of anal preservation surgery, meanwhile can the authors give more details about new delivery methods, such as intensity-modulated radiotherapy (IMRT)?

**Response:** In the page no. 4, We have explained about the new delivery method for radiotherapy such as IMRT in detail, and compared it with the another delivery method 3DCRT.

**2 :** In the part of Chemotherapy, could the authors present the neoadjuvant and adjuvant regimens with separate effects? After all, neoadjuvant therapy is becoming more and more common nowadays.

**Response:** Neoadjuvant and adjuvant regimens with their separate effects has been added in the page no 7-8.

**3:** Can the authors describe the long-term effects of Immunotherapy therapy, the shortcomings?

**Response:** Shortcomings and long-term effects of each immunotherapeutic approach has been added in details in page no. 14-15.

**4:** Can the authors compare the similarities and differences between these new promising treatments and which one holds the most promise?

**Response:** In the other approaches the new promising therapies has been grouped based on their similarities and differences, and the most promising one has been added accordingly in page no. 22-23.