

Peer Review File

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Reviewer A

Line 96, 198, 280, 368 Typo: “grade tree... adverse events” Do the authors mean “grade three”? This typo is seen throughout the manuscript in many sections.

Rely: We are very sorry for the mistake! We have corrected these spelling errors.

Chang in the text: we have modified our text as advised (see Page 1, 5, 10, 14, 18-19, line 12, 106, 211, 294, 298, 403, 415-416)

Line 233-234: Authors should consider providing citations for FDA or Guideline-based recommendations throughout the manuscript.

Rely: Thank you for your suggestion! We have added website of National Cancer Institute, where you can find recommendations for FDA as an adjuvant therapy for urothelial carcinoma.

Chang in the text: we have added website of National Cancer Institute (see Page 11, line 249)

Tables: Authors should organize tables better - specifically “Study Regimen” to clarify which NCT is associated with each regimen. When listed in a continuous column without lines or more spacing, it can be hard to delineate which regimen belongs to which study in some tables.

Rely: Thank you for your suggestion! We have modified the table to make it simpler and more organized.

Chang in the text: we have modified our text as advised (see Page 32-33, line 755-761; line 765-771)

Methods Section: Authors must provide more detailed inclusion/exclusion criteria in this section, as Table 1 is insufficient. It would be helpful to see the total number of studies included in the methods section. Along with any criteria that are pertinent to their search. The section starts with “May 2023” and seems out of context or incomplete, provide the complete study/search timeline.

Rely: Thank you very much! The description of this section is indeed not detailed enough. We have added specific inclusion/exclusion criteria, improved the search timeline, and language selection, and made modifications to Table 1.

Chang in the text: we have modified our text as advised (see Page 2, line 32-38; Page 4, line 75-81; Page 28, line 721-722)

The authors may consider being more critical/discuss the limitations of various studies provided throughout the manuscript.

Rely: Thank you for your suggestion! We have mentioned some research shortcomings and areas for improvement, respectively in chapters AC (see Page 8, line 171-173), neoadjuvant immunotherapy (see Page 11, line 231-232) and chemotherapy combined with immunotherapy (see Page 14, line 308-310). However, there are indeed some suggestions that are relatively vague and not profound enough. Therefore, we have added some comments and made the following modifications.

Chang in the text: we have added some research evaluations and suggestions in the neoadjuvant immunotherapy (see Page 10, line 221-223), chemotherapy combined with radiotherapy (see Page 17-18, line 378-383) and continuous and combined therapy (see Page 20, line 435-439) chapters, respectively.

This review would be greatly improved with a “future directions” section to expand on the future of these treatments, particularly ADC medicines, which the authors hone in on as most promising. The conclusion on ADC reads as inadequate/incomplete.

Rely: Thank you very much! This is a very helpful suggestion! We have expanded the continuous and combined therapy section based on your valuable suggestions and added the latest studies progress on ADC drugs. Please refer to the following instructions for details.

Chang in the text: we have added some data in the novel combined immunization regimen (see Page 16, line 344-357), chemotherapy combined with radiotherapy (see Page 17-18, line 381-383) and continuous and combined therapy (see Page 18-20, line 404-413; line 419-429) chapters, respectively.

Lines 129-130 + Biomarkers in general: Provide specific examples and statistical analyses, meaning are there any validated nomograms or cutoffs for these scores that are in the studies that are being referenced (ie, COXEN score)? Mentioning clinical significance without specifics on how this is applied or what specific statistical analyses have been done, leads to questioning the actual significance of this.

Rely: Thank you for your suggestion! The lack of statistical data for this COXEN score indeed reduces its credibility. Therefore, after rereading the research article, we added corresponding data, including its sensitivity and specificity, as follows:

Chang in the text: we have added some data in NAC chapters (see Page 7, line 141-144)

Reviewer B

In this paper authors present a contemporary review of perioperative systemic therapy for urothelial carcinoma of the bladder surrounding radical cystectomy, including neoadjuvant and adjuvant treatment with chemotherapy, immunotherapy, radiotherapy and relevant combinations. They also summarize ongoing trials in this space.

However there is almost no detail provided on the methodology of their search criteria, and in fact the methods section of the manuscript is only 1 sentence long. They do mention this is a narrative review and not systematic. There is no mention of the types of articles included in the search strategy (for example only randomized trials?), quality of/risk of bias of included articles, date range of included articles, databases searched, and languages included. They do include a narrative review checklist but the details are not reported in the manuscript. These details would need to be included prior to considering for publication.

Rely: Thank you very much for your valuable suggestion! The description of this section is indeed not detailed enough. We have added specific inclusion/exclusion criteria, improved the search timeline, and language selection, and made modifications to Table 1.

Chang in the text: We have modified our text as advised (see Page 2, line 32-38; Page 4, line 75-81; Page 28, line 721-722)

Further, the manuscript could be improved if authors provided a summary at the end of the remaining knowledge gaps of appropriate sequencing of systemic agents in MIBC, and which ongoing trials may address these knowledge gaps.

Rely: Thank you for your suggestion! We have added comments on the shortcomings of some studies and pointed out directions for improvement as well as research that can be referenced. Please refer to the modifications below for details.

Chang in the text: We have added some data in neoadjuvant immunotherapy (see Page 10, line 221-223), chemotherapy combined with immunotherapy (see Page 14, line 310-311) and continuous and combined therapy (see Page 20, line 435-439) chapters, respectively.