

## Peer Review File

Article information: <https://dx.doi.org/10.21037/tau-23-124>

### Reviewer A

1) Lines 92-94: TURBT as a solo modality is not recommended as the standard of care in patients with MIBC. The authors may want to rewrite this sentence to avoid misunderstanding by the readers.

Reply 1: Thanks! We have modified our text as advised (see Page 3, line 99-100)"

---

Changes in the text: *But as a solo modality, TURBT should not be recommended as the standard of care in patients with MIBC.*

2) ##Chemotherapy: The authors may want to summarize chemo agents used as a radiosensitizer for TMT.

Reply 2: Thanks! We have modified our text as advised (see Page 4, line 127-129)"

---

Changes in the text: *Chemotherapy agents used as radiosensitizers for TMT include gemcitabine, mitomycin C, fluorouracil/cisplatin, etc.*

### Reviewer B

The Authors reported data on the current evidence regarding bladder-sparing approaches for MIBC. Although authors should be commended for their work since it investigates an important topic, there are many issues that limit the quality of the manuscript in its current form.

Major

- In the introduction section, authors stated: "TMT is a well-tolerated and offers a curative alternative approach to RC for selected localized MIBC patients." Please provide reference for this statement and more important, in which patient it has been described to be well-tolerated? How well-tolerated has been defined?

Reply 3: Thanks! We have provided the reference No. (11).

"In which patient it has been described to be well-tolerated? How well-tolerated has been defined?"

Reply 4: Patient selection and the curative effect of TMT are described in detail in the later part of the article.

- In the introduction section authors stated:” Several organizations, including the European Association of Urology (EAU) and the American Urological Association (AUA), have updated the guidelines to support the application of chemotherapy combined with RT in selected MIBC patients”. This statement is imprecise since EAU guidelines support the use of bladder-sparing treatment surgeries only in patients unfit for or who declined RC. Please clarify this statement.

Reply 5: Thanks for your suggestion! We have modified our text as advised (see Page 3, line 74)"

---

Changes in the text: *Several organizations, including the European Association of Urology (EAU) and the American Urological Association (AUA), have updated the guidelines to support the application of chemotherapy combined with RT in selected MIBC patients unfit for or who declined RC*

- TURBT section: the authors should also discuss that about 20% of MIBC have nodal involvement at final pathology. Therefore, the staging ability and the potential therapeutic effect of an extended pelvic lymph node dissection (ePLND) is missed in a TURBT-only approach.

Reply 6: Thanks for your suggestion! We have modified our text as advised (see Page 3, line 96-100)"

---

Changes in the text: *It is worth noting that about 20% of MIBC have nodal involvement at final pathology. Therefore, the staging ability and the potential therapeutic effect of an extended pelvic lymph node dissection (ePLND) is missed in a TURBT-only approach. Thus, as a solo modality, TURBT should not be recommended as the standard of care in patients with MIBC.*

- In its current form, this SR is not informative for the reader. Authors should provide tables for each of the sections presented in the manuscript, providing the results and endpoints of each study included

- Another important element to discuss is the difficulty in comparing outcomes among studies. Please see and discuss this paper in which has been highlighted the lack of common endpoints among trials (PMID: 34840076)

Reply 7: Thanks for your suggestion! We have modified our text as advised (see Page 8, line 241-245)"

---

Changes in the text: *Finally, the difficulty in comparing outcomes among studies should be considered. Despite preliminary findings are encouraging, harmonization of terminology and definition of clinical endpoints among trials will be mandatory to correctly assess the potential role of CRT and immunotherapy combination as bladder-sparing solution in routine clinical practice (49). (PMID: 34840076)*

- Again, in the conclusion section, the authors stated that TMT is a well-tolerated treatment, however, there is no information regarding the safety profile of TMT. Thus, the authors should provide results about the safety profile of TMT if they want to conclude their manuscript in that way.

- Along all the sections there are many important papers missing. It is not clear how the authors decide to include or not the studies herein presented. Although it is a narrative review it should be informative how many studies were not included and how presented studies have been selected.

Minors:

- In the background and objective section of the abstract, the authors stated “TMT is a well-tolerated and offers a curative alternative approach to radical cystectomy (RC) for selected localized muscle invasive bladder cancer (MIBC) patients”. This statement should be the conclusion of the abstract rather than the background description. In the background section the authors should describe in which disease and which patient TMT has been investigated.

Reply 8: Thanks for your suggestion! We have modified our text as advised (see Page1, line 27-28)"

Changes in the text: *In recent years, the application of less-invasive “bladder-sparing” trimodal therapy (TMT) in selected muscle-invasive bladder cancer (MIBC) patients unfit for or who declined radical cystectomy (RC) has been increasing.*

## Reviewer C

### 1. Table 1

Please note that “Timeframe” means Timeframe of publication of the retrieved references, the current information should be revise.

Timeframe↵	20–30 July 2022↵
------------	------------------

Reply 1: we have modified our text as advised (see Page 15, line 468)

### 2. References/Citations

There are 2 reference lists in the file, please keep the correct one and delete another one.

\*Please note that there are 52 citations in the text.

Reply 2: we have modified our text as advised.