

Peer Review File

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Reviewer Comments

Reviewer A

Comment 1: Abstract, line 58

Decades in first line treatment of advanced (UC) patients → Decades in first line treatment of advanced urothelial carcinoma (UC) patients

Reply 1: Correction made both in the article manuscript (Abstract) and Metadata section.

Reviewer B

Comment 1: Roche has voluntarily withdrawn the US indication of atezolizumab (Tecentriq) for the treatment of adults with advanced or metastatic urothelial carcinoma

Reply 1: Added sentence and reference, in agreement with the comment (Lines 279-281).

Comment 2. Bempegaldesleukin phase III study has failed and its further development has stopped

Reply 2: Added sentence and reference, in agreement with the appropriate comment (Lines 384-387).

Reviewer C

Comment 1: Would review the manuscript and make sure generic drug names are not capitalized (eg line 181 atezolizumab, line 211 durvalumab)

Reply 1: Multiple corrections made throughout the text and highlighted.

Comment 2: Line 279 - progressing after, not to?

Reply 2: Expression changed in agreement with the reviewer's preference.

Comment 3: Line 356-258 - would cite a few sources that have suggested UC with FGFR mutations is less susceptible to ICI (I know that to be true as well but should be cited).

Reply 3: Appropriate references added (Ref 50-52).

Comment 4: I would emphasize the need for strategies in cisplatin ineligible patients. Obviously EV/pembro is on the immediate horizon which you covered. But would also would incorporation mention of ongoing trials like PemCab (NCT03534804) which combines cabozantinib and pembro in cis ineligible 1st line therapy.

Reply 4: Emphasis on the need for strategies in cisplatin eligible patients highlighted at the very top of the chapter: *Innovative approaches and drugs under clinical*

development (Lines 315-316). Added content highlighting ongoing research in the field of TKI + ICI (Lines 336-342).

Comment 5: You also didn't mention sacituzumab but it deserves mention as both an FDA approved agent on its own in mUC but also there is data from ongoing trials showing its efficacy in combination with immunotherapy like TROPHY-U-01 Cohort.

Reply 5: Added data on sacituzumab govitecan and TROPHY-U-01 trial (Lines 330-336).

Comment 6: The scope of this journal is very broad so perhaps this type of article is acceptable but given that it is being reviewed by a journal centered around palliative medicine, it may be worth emphasizing the improvement in QoL offered by immunotherapy from a side effect but also schedule standpoint that is not possible with antibody drug conjugates or platinum doublet chemotherapy.

Reply 6: Added relevant comment on QoL improvement (Lines 141-145).