



SDI Review Form 1.6

Journal Name:	<a href="#">Journal of Advances in Medicine and Medical Research</a>
Manuscript Number:	Ms_JAMMR_45373
Title of the Manuscript:	The assessment of HE4 in premalign and malign urothelial tumors
Type of the Article	Original Research Article

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This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound. To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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**PART 1: Review Comments**

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<p><b>Compulsory</b> REVISION comments</p>	<p>I have some major questions concerning the study-population, see all my comments below (in the very end)</p> <p>I believe this is a study that is fairly fine done and good presented, well written, good English (except a few spelling mistakes). As mentioned, I have although some major concerns about the study-population and also, partly due to the huge exclusion of tumour-material, doubts about the final conclusion in this study.</p> <p><b>Specific comments from reviewer</b></p> <p><b>Background:</b> - Bladder cancer cancer (BC) has been the most common urinary tract malignancy in the USA. <b>Comment: "Cancer cancer" Probably just a mistake. And It's better to use the terminology UBC (urinary bladder carcinoma) (Bladder can in some instances be mistaken for Gallbladder)</b></p> <p><b>Materials and Methods</b> -The histologic classification of tumors were made on the basis of guidelines from The 2016 WHO Classification of Tumours of the Urinary System (13). <b>Comment: According to this sentence, and the fact that collection of material was done from 2010-2016, there must have been a reevaluation of the histological slides; I think it's important that it is clearly stated in the text. By reading further(patients excluded due to lack of information in the pathology report) I realize there was no reevaluation, the fact that the tumor were collected 2010-2016 and not reevaluated and still was classified according to the 2016 system is unfortunately not trustworthy – You need to explain this.</b></p> <p>-The H-scores for tumors with multiple cores were averaged. <b>Comment: I don't understand what You in this context mean with "core" (the material was from TUR (not core-biopsies), maybe You mean different pieces whit tumor on the same slide?)</b></p> <p><b>Results</b> For the rest of 163 cases, there were 11 PUNLMP, 97 LGPUC, and 55 HGPUC cases. Among them 5 PUNLMP, 16 LGPUC, 7 HGPUC, and 27 invasive UC in which 9 of them had muscularis propria invasion were succesfully stained with anti-HE4 antibody. There were 45 male (81.8%) and 10 female (18.2%) patients. Patients age was ranged between 40 to 89 years (mean 68.06 ± 10.82). <b>Comment: From 163 cases in total to suddenly 55 cases left for IHC? What happened to the rest? You must explain here, You have excluded close to 2/3 of the initial study-population without any trustworthy explanation? This must of course affect the outcome in this study.</b></p>	



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	<p><b>Discussion</b> HE4 expression seen in our <b>PUNLMP cases deserve attention</b>. Higher expression rate seen in PUNLMP compared to overt malignant cases in this study can be explained with the low number of the study population in this group. On the other hand, HE4 positivity might predict cases that would progress to a higher grade lesion as well, as the long-term outcome of PUNLMP demonstrates a broad range of recurrence and progression rates (14). This study had some limitations which had to be pointed out. The small patient population was the most important limitation. Secondly, cases from the <b>urothelial proliferation of uncertain malignant potential were not included</b>, as cases had been disappeared on the block while taking the section for staining.</p> <p><b>Comment: First You give PUNLMP special attention and then You say “cases from urothelial proliferation of uncertain malignant potential were not included” ? Do You think it’s not the same as PUNLMP?</b></p>	
<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments		

**PART 2:**

	<b>Reviewer’s comment</b>	<b>Author’s comment</b> (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<b>Are there ethical issues in this manuscript?</b>	<i>(If yes, Kindly please write down the ethical issues here in details)</i>	

**Reviewer Details:**

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