Reviewer A

Comment 1: The background section in the abstract can be rephrased and written better to deliver the objective of the manuscript.
Reply 1: The manuscript has been revised as required.
Changes in the text: Lines 8 to 9

Comment 2: Anoikis-related genes (ARGs) and their importance should be defined initially in the manuscript
Reply 2: The manuscript has been revised as required.
Changes in the text: Lines 45 to 47

Comment 3: Define the terms like TIDE and TCIA and then the abbreviations should be used for easy comprehension.
Reply 3: Abbreviations are defined in manuscripts.

Comment 4: In the Introduction section, a figure to explain anoikis-related genes and their
mechanism/function to clear the concept would be better.
Reply 4: The manuscript has been revised as required.
Changes in the text: Lines 45 to 53

Comment 5: Since low-risk patients respond better to immunotherapy, what about Antibody-drug conjugates (ADCs)? Were the patients treated with ADCs also studied?
Reply 5: Your suggestion is very important. We will explore this question further in the following research.

Comment 6: What about Erdafitinib? Does that have a role in low-risk or high-risk patients?
Reply 6: In our data analysis, no differences in the sensitivity of erdafitinib for patients with different risk scores were found.

Comment 7: The patients with high risk are sensitive to chemotherapeutics and/or targeted agents. (Because Dasatinib, Foretinib, and Talazoparib all are targeted agents and NOT
chemotherapeutic agents)
Reply 7: Thank you very much for your suggestion. We have made revisions in the manuscript.
Changes in the text: Lines 28 to 31, 286 to 287

Comment 8: A table in the discussion section about the 9 ARGs should be added for better and concise understanding.
Reply 8: Model-related genes have been fully discussed in the manuscript. Changes in the text: Lines 235 to 277

Comment 1: Include Statistical Analysis in Methods Section.
Reply 1:
2.9 Statistical analysis
The statistical analysis was performed using R software (version 4.1.2). The chi-square test was used to analyse differences in patients, with Kaplan-Meier analysis and log-rank analysis used to assess patients' overall survival (OS) and Progression-Free-Survival (PFS). The Wilcoxon test was used to check the deviation between the components. A P-value <0.05 was considered statistically significant.

Comment 2: Figures and subfigures should be cited consecutively.
Reply 2: The manuscript has been revised as requested.

Comment 3: Reference #61 and #65 are the same. Delete one of them and number the rest of the references consecutively in the order.
Reply 3: It has been modified as required.

Comment 4: You refer to "studies" with only one literature citation several times.
362   tropomyosin (52, 53), is abundant in numerous cell types (54). Numerous studies
363   indicate that *TPM1*—a cancer suppressor gene—is expressed at low levels in a variety
364   of tumor cells (55). The findings regarding this gene and bladder cancer are

327   Studies indicate that *CASP6* is primarily responsible for encoding the Caspase-6
328   protein, and its expression is negatively correlated with tumor development (24). In
338   *INHBB* in renal cell carcinoma, pancreatic cancer, and lung cancer (28, 29). And some
339   studies even consider it to be a tumor-inhibiting factor (30). Despite this, a large
343   was associated with a poor prognosis in patients with bladder cancer; similar findings
344   have been reported in some other studies on gastric cancer (33). *KLF12* is a member
Reply 4: It has been modified as required.

Comment 5: In the sentence below, you refer to "study" but have more than one citation.
345   of the Krüppel-like factors (KLFs) family (34). The study found that *KLF12* was
346   abnormally expressed in a variety of tumors (35-37). In addition, *KLF12* plays a
Reply 5: It has been modified as required.

Comment 6: Add the group name/title/unit on the X-axis of Figure 2C.
Reply 6: Figure 2 has been modified. The illustrations in the manuscript have been updated.

Comment 7: Add a space between "survivalall", "survivaltrain", and "survivaltest" in Figure 3A-C. The same goes for Figure 3D-F.

Reply 7: Figure 3 has been modified. The illustrations in the manuscript have been updated.

Comment 8: Indicate whether it is PAC3 or RAC3.

254 *RAC3* and *INHBB* (Figure 4D). Four genes screened were found to be significantly
255 differentially expressed between tumor and normal tissues (*FASN*, *PAC3*, *TPM1*, and
256 *TGFBR3*) (Figure 4E). HPA analyze package was used to count the

Reply 8: RAC3. The error has been fixed.

**Comment 9:** According to Figure 4G, these should be TGFBR3.

259 (IHC) results of F*ASN, RAC3*, and *TPM1* and the gene expression results by analyzing
260 the statistical results, but no significant differences between the IHC results of
261 *TGFBR3* in normal tissue and tumor tissue. Then, the detailed IHC of *FASN*, *RAC3*, and
262 *TPM1* was displayed (Figure 4G).

Reply 9: TGFBR3. The error has been fixed.

Comment 10: There is no * in Figure 4D.

Reply 10: Figure 4 has been modified. The illustrations in the manuscript have been updated.

Comment 11: Seems the symbol (−) is missing in Figure 4D.
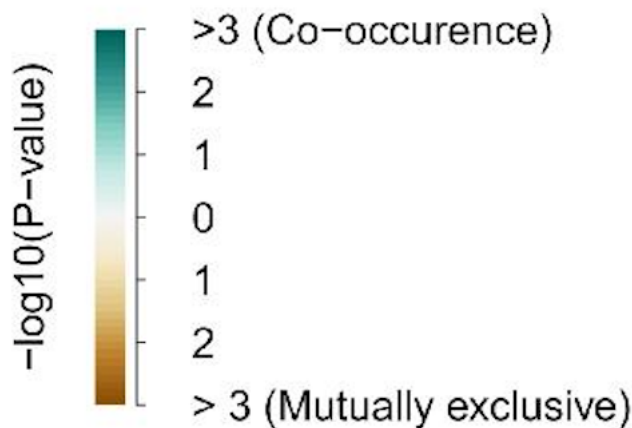
Reply 11: Figure 4 has been modified. The illustrations in the manuscript have been updated.

Comment 12: Change "urothelial cancer" in Figure 4F to vertical.

Reply 12: Figure 4 has been modified. The illustrations in the manuscript have been updated.

Comment 13: Add the scale bars of Figure 4G.

Reply 13: We've added that section to the legend.

All images in Figure 4E are magnified by a factor of 40.
FASN
Tumor: https://www.proteinatlas.org/ENSG00000169710-FASN/pathology/urothelial+cancer#ihc
Normal: https://www.proteinatlas.org/ENSG00000169710-FASN/tissue/urinary+bladder
RAC3
Tumor: https://www.proteinatlas.org/ENSG00000169750-RAC3/pathology/urothelial+cancer#ihc
Normal: https://www.proteinatlas.org/ENSG00000169750-RAC3/tissue/urinary+bladder
TGFBR3
Tumor: https://www.proteinatlas.org/ENSG00000069702-TGFBR3/pathology/urothelial+cancer#ihc
Normal: https://www.proteinatlas.org/ENSG00000069702-TGFBR3/tissue/urinary+bladder

Comment 14: Add the age unit in Figure 5A.
Comment 14: The figure has been revised as requested.

Comment 15: Indicate whether it is KAGG or KEGG.
630   **FIGURE 6** Pathway enrichment analysis results. **(A)** The KAGG pathway enriched in
631   the low-risk group; **(B)** KAGG pathway enriched in high-risk groups; **(C)** Enrichment
Reply 15: KEGG. The error has been fixed.

Comment 16: Explain what *** in Figure 7A and * in Figure 7F mean in the caption.
Reply 16: We've added that to the legend.

Comment 17: Red usually represents high-risk. Please update Figure 7D and 7E.
Reply 17: Figure 7 has been modified. The illustrations in the manuscript have been updated.

Comment 18: According to Figure 8G, this should be Entospletinib.
312   The results of the drug sensitivity analysis revealed that patients with higher risk
313   scores were more sensitive to common chemotherapeutic drugs (Foretinib, Taselisib,
314   Cisplatin, Staurosporine, Trametinib, Dasatinib, Entosplenosporine, Talazoparib, and
315   5-Fluorouracil) (Figure 8). These results could help in providing more precise
Reply 18: Figure 8 has been modified. Let's refer to Figure 8 as a whole. The illustrations in the manuscript have been updated.

Comment 19: Provide figure caption for each subfigure 8A-8I.
Reply 19: Figure 8 has been modified. Let's refer to Figure 8 as a whole. The illustrations in the manuscript have been updated.