Urology Research, 2025, Volume 3, Issue 1
https://ojs.bbwpublisher.com/index.php/UR
Online ISSN: 2981-8230

Exploring the Adverse Reactions and Risk Factors of Toripalimab in the Treatment of Urothelial Carcinoma

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Abstract: *Objective:* This study aims to investigate the adverse reactions and risk factors associated with toripalimab in the treatment of urothelial carcinoma. *Methods:* The clinical data of 63 patients with urothelial carcinoma who received toripalimab treatment in our hospital from June 2021 to January 2025 were retrospectively analyzed. Patient data, including baseline characteristics (age, gender, Eastern Cooperative Oncology Group [(ECOG] score, comorbidities), treatment history (chemotherapy, radiotherapy), and adverse reactions, were selected through the hospital's electronic medical record system. *Results:* Among the 63 patients, 49 (77.78%) experienced toripalimab-related adverse reactions, with skin rash occurring most frequently. Univariate analysis showed that age, comorbidities such as hypertension, diabetes, and bronchial asthma, as well as the use of combined radiotherapy and chemotherapy, were significantly associated with toripalimab-related adverse reactions (all $P < 0.05$). Multivariate logistic regression analysis revealed that combined chemotherapy was an independent risk factor for toripalimab-related adverse reactions ($P < 0.05$). *Conclusion:* Immune-related adverse reactions observed during toripalimab treatment for urothelial carcinoma include skin rash, elevated transaminase levels, abnormal renal function, anemia, etc. Factors influencing these reactions include age, underlying diseases, and combined radiotherapy and chemotherapy, among which combined chemotherapy is an independent risk factor for adverse reactions. When using toripalimab in clinical practice, it is essential to follow the approved indications on the label, monitor patients for adverse reactions during treatment, and intervene effectively to ensure patient safety.

Keywords: Toripalimab; Urothelial carcinoma; Risk factors; Logistic regression analysis; Adverse reactions

Online publication: April 2, 2025

1. Introduction

Urothelial carcinoma, including bladder cancer, renal pelvis cancer, ureteral cancer, and urethral cancer, is one of the common malignancies of the urinary system. Its incidence and mortality rates have been increasing year by year.

According to the latest domestic research statistics, the incidence of urothelial carcinoma ranks 13th among all cancer patients, making it a significant public health issue [1]. In recent years, immunotherapy, primarily focused on immune checkpoint inhibitors, has brought new hope for the treatment of urothelial carcinoma. This therapeutic approach can effectively activate anti-tumor immunity and reduce the immune escape rate of tumors [2], offering hope to patients. Toripalimab is China's first domestically produced programmed death receptor-1 (PD-1) monoclonal antibody drug approved for market. By disrupting the immunosuppressive effects of the PD-1 signaling pathway, it restores T cell function, targets tumor cells, and regulates autoimmunity. The emergence of toripalimab has improved the treatment effectiveness of cancer patients to a certain extent, prolonged their survival time, and enhanced their quality of life [3,4]. However, there is limited research on its adverse reactions in practical applications. Therefore, this study adopts a retrospective approach to analyze the adverse reactions and risk factors of toripalimab in treating urothelial carcinoma, aiming to provide a reliable theoretical foundation for clinical medication administration.

2. Materials and methods

2.1. General information

A retrospective analysis was conducted on the clinical data of 63 patients with urothelial carcinoma who received toripalimab treatment in our hospital from June 2021 to January 2025. Inclusion criteria: (1) Aged between 18 and 85 years old; (2) Patients were diagnosed with locally advanced/metastatic urothelial carcinoma after cytological or histological examination [5]; (3) All were treated with toripalimab (240 mg of toripalimab intravenously every two weeks); (4) Good function of important organs; (5) At least one measurable target lesion. Exclusion criteria: (1) Incomplete clinical data collection; (2) Combined with other types of bladder cancer besides urothelial carcinoma; (3) Previously received other types of PD-1 or PD-L1 drugs for treatment; (4) Suffering from severe underlying diseases; (5) Having toxic reactions caused by drugs other than toripalimab.

2.2. Data collection

Patient data, including basic information (age, gender, Eastern Cooperative Oncology Group [ECOG] score, comorbidities), treatment history (chemotherapy, radiotherapy), and adverse reactions, were selected through the hospital's electronic medical record system. The occurrence of adverse reactions includes the number of cases, types, severity, etc.

2.3. Criteria for determining adverse events

Based on the Common Terminology Criteria for Adverse Events (CTCAE), toripalimab-related adverse events were classified and graded as follows:

(1) Grade 1 (mild): asymptomatic or mild symptoms; observed only during clinical or diagnostic examinations; no treatment required.

(2) Grade 2 (moderate): requiring local or non-invasive therapy; age-related instrumental activities of daily living are limited.

(3) Grade 3 (severe): medically significant but not immediately life-threatening; requiring hospitalization or prolongation of hospitalization; disabling; limiting self-care.

(4) Grade 4 (life-threatening consequences): requiring urgent intervention.

(5) Grade 5: death related to adverse events [6,7].

2.4. Statistical analysis

SPSS 26.0 statistical software was used for data processing in this study. The count data involved were expressed as (*n*, %), and chi-square test analysis was performed. Logistic regression analysis was used to identify influencing factors. When $P < 0.05$, it indicated that the data had statistically significant differences.

3. Results

3.1. Incidence and types of toripalimab-related adverse events

Among the 63 patients, 49 patients (77.78%) experienced toripalimab-related adverse events, with a total of 60 occurrences. Grade 1 and 2 adverse events occurred 56 times, accounting for 93.33%, while Grade 3 and above adverse events occurred 4 times, accounting for 6.67%. The specific data are shown in **Table 1**:

Table 1. Incidence and types of toripalimab-related adverse events (*n*, %)

Types of adverse reactions	Severity level	Frequency of occurrence	Incidence rate (%)
Rash	Grade 1	15	25.00
Elevated transaminase levels	Grade 1	11	18.33
Abnormal renal function	Grade 2	7	11.67
Anemia	Grade 2	9	15.00
Neutropenia	Grade 1	5	8.33
Thrombocytopenia	Grade 1	4	6.67
Loss of appetite	Grade 1	4	6.67
Blood clot formation	Grade 2	1	1.67
Muscle weakness	Grade 3	2	3.33
Interstitial pneumonia	Grade 3	2	3.33
Total		60	100.00

3.2. Univariate analysis of toripalimab-related adverse events

Univariate analysis showed that age, comorbidities such as hypertension, diabetes, bronchial asthma, and combined radiotherapy and chemotherapy were the main factors associated with toripalimab-related adverse events (all $P < 0.05$). However, gender, primary tumor location, ECOG score, and comorbid chronic bronchitis were not significantly associated with adverse events (all $P > 0.05$). Specific data are presented in **Table 2**:

Table 2. Univariate analysis of toripalimab-related adverse events (*n*, %)

Factors		Group without adverse reactions (*n* = 14)	Group with adverse reactions (*n* =49)	χ^2-value	*P*-value
Age	> 65	10	19	4.673	0.031
	≤ 65	4	30		
Gender	Male	6	26	0.454	0.501
	Female	8	23		

Table 2 (Continued)

Factors		Group without adverse reactions (n = 14)	Group with adverse reactions (n =49)	χ^2-value	P-value
Location of the primary tumor	Bladder cancer	9	31	0.828	0.843
	Renal pelvis cancer	3	13		
	Ureteral cancer	2	4		
	Others	0	1		
ECOG score	0 points	7	29	0.284	0.594
	1 point	7	20		
Hypertension	Combined	3	30	6.914	0.009
	Not combined	11	19		
Diabetes mellitus	Combined	5	34	5.236	0.022
	Not combined	9	15		
Chronic bronchitis	Combined	10	21	3.556	0.059
	Not combined	4	28		
Bronchial asthma	Combined	2	26	6.631	0.010
	Not combined	12	23		
Combined radiotherapy	Combined therapy	4	31	5.308	0.021
	Not combined therapy	10	18		
Combined chemotherapy	Combined therapy	5	33	5.998	0.014
	Not combined therapy	9	16		

3.3. Multivariate logistic regression analysis of toripalimab-related adverse reactions

Using the occurrence of adverse reactions as the dependent variable (occurred = 1, did not occur = 0), and with age, comorbid hypertension, diabetes, bronchial asthma, as well as combined radiotherapy and chemotherapy as independent variables, values were assigned (**Table 3**). The results of the multivariate logistic regression analysis showed that combined chemotherapy is an independent risk factor for toripalimab-related adverse reactions ($P < 0.05$), as shown in **Table 4**.

Table 3. Independent variable assignment table

Independent variables	Value assignment
Age	65 years old = 1, ≤ 65 years old = 0
Comorbid hypertension	With comorbidity = 1, without comorbidity = 0
Comorbid diabetes	With comorbidity = 1, without comorbidity = 0
Comorbid bronchial asthma	With comorbidity = 1, without comorbidity = 0
Combined radiotherapy	Combined = 1, not combined = 0
Combined chemotherapy	Combined = 1, not combined = 0

Table 4. Multivariate logistic regression analysis of toripalimab-related adverse reactions

Related factors	β-value	SE	Wald χ^2-value	*P*-value	OR-value	95% CI
Age	0.051	0.694	0.005	0.941	1.053	(0.271, 4.104)
Comorbid hypertension	0.149	0.776	0.037	0.848	1.161	(0.254, 5.315)
Comorbid diabetes	1.153	0.802	2.066	0.151	0.316	(0.066, 1.521)
Comorbid bronchial asthma	0.211	0.702	0.091	0.763	1.235	(0.312, 4.891)
Combined radiotherapy	0.696	0.777	0.803	0.370	0.498	(0.109, 2.286)
Combined chemotherapy	2.351	1.106	4.517	0.034	1.095	(0.011, 0.833)

4. Discussion

Urothelial carcinoma is a common malignancy of the urinary system with poor prognosis and high recurrence and metastasis rates [8]. Although radiotherapy, chemotherapy, and other means are currently used clinically to treat patients with unresectable advanced urothelial carcinoma, which can improve the prognosis of patients to some extent, the long-term survival rate is still at a low level, and further treatment options need to be explored.

Currently, PD-1/PD-L1 immune checkpoint inhibitors have achieved good results in studies on lung cancer, liver cancer, etc. [9], providing new ideas for the treatment of malignant tumors. Toripalimab is a recombinant humanized anti-PD-1 monoclonal antibody injection with a unique dual mechanism of action. It not only binds to PD-1 to block its binding to PD-L1, significantly increasing its killing effect on tumors but also induces endocytosis of PD-1, further improving the T-cell response to antigenic stimulation and controlling tumor development [10]. However, there are few studies on the safety of toripalimab. Therefore, this study focuses on the adverse reactions of toripalimab in clinical treatment and uses retrospective analysis to explore the influencing factors of toripalimab-related adverse reactions. The results showed that among 63 patients, 49 experienced toripalimab-related adverse reactions (77.78%), with rash occurring most frequently. As a common adverse reaction, rash may be closely related to increased PD-1 expression levels in skin tissue and T-cell activation, which is consistent with the typical toxicity profile of PD-1 inhibitors. Therefore, when using toripalimab for clinical treatment, attention should be paid to rash prevention measures and strengthened monitoring [11].

Univariate analysis showed that age, comorbid hypertension, comorbid diabetes, comorbid bronchial asthma, and combined radiotherapy and chemotherapy are the main factors for toripalimab-related adverse reactions ($P < 0.05$ for all). The reason may be that elderly patients often experience immune senescence, and the body itself exhibits T-cell dysfunction, which may lead to immunotherapy-induced toxicity. In patients with metabolic diseases, insulin resistance and vascular endothelial injury alter the metabolism and migration ability of immune cells in the body. Respiratory diseases such as asthma may affect the immune microenvironment due to Th2 immune deviation, intensifying toxic reactions [12]. Additionally, multivariate logistic regression analysis showed that combined chemotherapy is an independent risk factor for toripalimab-related adverse reactions ($P < 0.05$). Chemotherapy drugs such as cisplatin and gemcitabine can damage the mucosal barrier and induce cell damage, releasing autoantigens. These drugs may produce a synergistic immunostimulatory effect with toripalimab, further leading to toxicity superposition [13]. In summary, when using toripalimab for clinical treatment, it is important to follow the approved indications on the package insert, closely monitor patients for adverse reactions during

treatment, and intervene effectively once they are detected to ensure patient safety.

5. Conclusion

In conclusion, the immune-related adverse reactions observed during the treatment of urothelial carcinoma with toripalimab include rash, elevated transaminase levels, abnormal kidney function, anemia, etc. Analysis shows that age, underlying diseases, and combined radiotherapy and chemotherapy are influencing factors, with combined chemotherapy being an independent risk factor for adverse reactions. However, this study has some limitations. For example, the small sample size may cause data deviation, and the adverse reaction grading and correlation with dosage are not clear, limiting the assessment of toxicity severity. Future research will further optimize the study protocol to provide a strong theoretical foundation for the safety study of toripalimab in the treatment of urothelial carcinoma.

Funding

2024SF-YBXM-195

Disclosure statement

The authors declare no conflict of interest.

References

[1] Wei Z, 2022, Evaluation of the Efficacy and Safety of PD-1 Inhibitors in the Treatment of Advanced Urothelial Carcinoma, dissertation, Chongqing Medical University.

[2] Liu W, Shen H, 2023, Efficacy of PD-1 Monoclonal Antibody Combined with GC Chemotherapy in the Treatment of Advanced Urothelial Carcinoma and its Impact on Tumor Malignancy. Chongqing Medicine, 52(21): 3274–3278 + 3282.

[3] Wang Y, Tang L, Huang L, 2025, Effect of Toripalimab Combined with Radiotherapy and Chemotherapy in the Treatment of Stage III Non-Small Cell Lung Cancer and Its Influence on Tumor Markers. Rational Drug Use in Clinic, 18(01): 76–78 + 85.

[4] Su L, Xu Q, Wan S, et al., 2024, Analysis of the Efficacy and Safety of Toripalimab in the Comprehensive Treatment of Bladder Tumors. Journal of Chongqing Medical University, 49(06): 740–744.

[5] Deng Q, Li Z, Li C, et al., 2024, Research Progress of Antibody-Drug Conjugates Combined with Immunosuppressants in the Treatment of Locally Advanced or Metastatic Urothelial Carcinoma. Modern Medicine & Health, 40(19): 3353–3358.

[6] Chen Y, Jing T, Zhao M, 2023, Clinical Characteristics Analysis of Adverse Drug Reactions Caused by Toripalimab. Anti-infection Pharmacy, 20(01): 18–22.

[7] Xi Y, Huang Y, Han Z, et al., 2024, Analysis of Adverse Reactions and Risk Factors of Tislelizumab in the Treatment of Urothelial Carcinoma. Practical Medicine and Clinical Remedies, 27(02): 102–106.

[8] Wei X, Chen Y, Jiang Q, 2024, Progress in Immunotherapy during the Perioperative Period of Bladder Urothelial Carcinoma. Laboratory Medicine and Clinic, 21(04): 547–551.

[9] Guo Y, Feng D, Zhong H, et al., 2025, Effects of PD-1 Inhibitors Combined with Reduced-Dose Chemotherapy on Immune Function and Platelets in Patients with Advanced Lung Cancer. Journal of North Sichuan Medical College, 40(02): 168–171.

[10] Gao G, Hua Y, Wang G, 2025, Comparison of the Effects of Different PD-1 Inhibitors Combined with Lenvatinib in the Treatment of Primary Liver Cancer. Modern Practical Medicine, 37(01): 18–21.

[11] Zhao Y, Guan F, Han Z, et al., 2023, Clinical Observation of Skin Immune-Related Adverse Reactions caused by Programmed Cell Death Protein-1 (PD-1) Inhibitors. Journal of Military Medical University of the People's Liberation Army, 45(22): 2352–2357.

[12] Wang Y, 2022, The Effect of PPI on the Efficacy of PD-1 Inhibitors in the Treatment of Liver Cancer—PSM analysis combined with Nomogram prognostic prediction analysis, dissertation, Guangxi Medical University.

[13] Wei J, Zheng Y, Zhang Y, et al., 2024, Comparison of the Efficacy of Neoadjuvant PD-1 Inhibitors Combined with Chemotherapy and Neoadjuvant Chemotherapy in the Treatment of Resectable Stage III Non-Small Cell Lung Cancer. Modern Oncology, 32(11): 2014–2019.

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