Proceedings of Anticancer Research, 2025, Volume 9, Issue 1
http://ojs.bbwpublisher.com/index.php/PAR
ISSN Online: 2208-3553
ISSN Print: 2208-3545

Clinical Efficacy and Safety Analysis of Toripalimab Combined with GC Chemotherapy for Advanced Urothelial Carcinoma

Song Xue[1], Dongli Ruan[2]*

[1]Xi'an People's Hospital (Xi'an Fourth Hospital), Xi'an 710000, Shaanxi Province, China

[2]Shaanxi Provincial People's Hospital, Xi'an 710000, Shaanxi Province, China

***Corresponding author:** Dongli Ruan, 745501416@qq.com

Abstract: *Objective:* To analyze the clinical efficacy and safety of toripalimab combined with the GC chemotherapy regimen in the treatment of advanced urothelial carcinoma. *Methods:* A retrospective study was conducted on 102 patients with advanced urothelial carcinoma treated at our hospital between March 2021 and August 2024. Based on treatment regimens, patients were divided into a chemotherapy group (n = 52) and a combination group (n = 50). The chemotherapy group received the GC chemotherapy regimen, while the combination group received GC chemotherapy combined with toripalimab. Both groups underwent 4–6 cycles of treatment based on patient tolerance. Clinical efficacy, immune-related factor levels, survival outcomes, and safety were observed and compared. *Results:* The disease control rate (DCR) and overall response rate (ORR) in the combination group were slightly higher than those in the chemotherapy group, but the differences were not statistically significant ($P > 0.05$). After treatment, levels of IFN-γ and IL-2 increased significantly, while VEGF levels decreased significantly in both groups ($P < 0.05$), with superior outcomes observed in the combination group ($P < 0.05$). Follow-up analysis showed progression-free survival (PFS) and median overall survival (OS) in the chemotherapy group were 5.19 and 10.15 months, respectively, compared to 8.24 and 18.23 months in the combination group, with statistically significant differences ($P < 0.05$). During treatment, the incidence of adverse reactions such as rash, immune-related pneumonia, and immune-related diarrhea was higher in the combination group than in the chemotherapy group ($P < 0.05$). However, the incidence of gastrointestinal reactions, fever, and leukopenia did not differ significantly between the two groups ($P > 0.05$). *Conclusion:* The use of toripalimab combined with the GC chemotherapy regimen for advanced urothelial carcinoma can effectively improve clinical outcomes and extend patient survival, with good overall safety. However, attention should be given to preventing adverse reactions such as rash and pneumonia during treatment.

Keywords: Urothelial carcinoma; Toripalimab; Chemotherapy; Survival; Efficacy; Safety

Online publication: February 13, 2025

1. Introduction

Urothelial carcinoma (UC) arises from the epithelial tissues of the renal calyces, renal pelvis, bladder, and ureters, and is one of the most common tumors, accounting for 5–10% of urinary tract malignancies. It is associated with poor prognosis and high recurrence and metastasis rates [1]. UC often presents without obvious early clinical symptoms, and most patients are diagnosed at an advanced stage, missing the optimal treatment window. For patients with advanced UC who cannot undergo surgical resection, systemic chemotherapy remains the primary treatment approach.

Clinical studies have shown that the gemcitabine-cisplatin (GC) chemotherapy regimen improves patient prognosis with a relatively low incidence of adverse reactions [2]. However, long-term survival outcomes following this regimen remain suboptimal, necessitating the exploration of more effective therapeutic strategies.

In recent years, immunotherapy has emerged as one of the most successful approaches for UC treatment and is now the standard of care for both in situ urothelial carcinoma and superficial bladder tumors [3]. This study retrospectively analyzed the clinical data of UC patients to evaluate the clinical efficacy and safety of immunotherapy combined with the GC chemotherapy regimen in treating advanced UC.

2. Materials and methods

2.1. General information

A retrospective study was conducted on 102 patients with advanced urothelial carcinoma treated at our hospital from March 2021 to August 2024. Based on treatment regimens, patients were divided into a chemotherapy group (n = 52) and a combination group (n = 50). In the chemotherapy group, there were 29 males and 23 females, aged 50–80 years, with an average age of (64.32 ± 6.22) years. Cancer types included ureteral cancer (6 cases), renal pelvic cancer (4 cases), bladder cancer (40 cases), and others (2 cases). The Karnofsky Performance Status (KPS) scores ranged from 65 to 90 points [4], with an average score of (74.91 ± 4.57) points. In the combination group, there were 30 males and 20 females, aged 52–80 years, with an average age of (65.01 ± 5.96) years. Cancer types included ureteral cancer (5 cases), renal pelvic cancer (5 cases), bladder cancer (39 cases), and others (1 case). KPS scores ranged from 63 to 90 points, with an average score of (76.14 ± 6.03) points. The baseline data of the two groups were comparable ($P > 0.05$). This study was approved by the hospital ethics committee.

2.2. Inclusion and exclusion criteria

Inclusion criteria:

(1) Pathologically confirmed urothelial carcinoma [5].

(2) Clinical stage III B to IV.

(3) Ineligible for surgery or showing recurrence/metastasis after surgery.

(4) Eastern Cooperative Oncology Group (ECOG) performance score of 0–2.

(5) KPS score ≥ 60 points.

(6) Estimated survival time ≥ 3 months.

Exclusion criteria:

(1) Severe damage to other vital organs.

(2) Autoimmune or hematological diseases.

(3) Brain metastasis.

(4) History of immunotherapy.

(5) Poor compliance or cooperation during treatment and follow-up.

Elimination criteria:

(1) Patients with an estimated survival quality of < 3 months.

2.3. Methods

The chemotherapy group received the GC chemotherapy regimen: gemcitabine (2,500 mg/m²) on days 1 and 8, and cisplatin (70 mg/m²) on day 2. Each chemotherapy cycle was 21 days.

The combination group received GC chemotherapy as described above, combined with immunotherapy using toripalimab (240 mg) every 2 weeks via intravenous infusion.

Both groups underwent 4–6 cycles of treatment based on patient tolerance. During cisplatin administration, adequate hydration was ensured to maintain urine output ≥ 2,000 mL/day. Blood counts and liver and kidney function were monitored regularly during chemotherapy. In cases of thrombocytopenia or leukopenia, treatment with hematopoietic growth factors was initiated. Symptomatic treatments, including fluid replacement and antiemetics, were provided for adverse reactions.

2.4. Observational indicators and evaluation criteria

The study assessed clinical efficacy, immune-related factor levels, survival outcomes, and safety in both groups:

(1) Clinical efficacy: Assessed according to the WHO criteria for solid tumors, including progressive disease (PD), stable disease (SD), partial response (PR), and complete response (CR). Disease control rate (DCR) = (SD + PR + CR cases) / total cases × 100%. Objective response rate (ORR) = (PR + CR cases) / total cases × 100% [6].

(2) Immune-related factor levels: Peripheral blood samples were collected before treatment and after 4 treatment cycles. Serum levels of interferon-gamma (IFN-γ), interleukin-2 (IL-2), and vascular endothelial growth factor (VEGF) were measured using enzyme-linked immunosorbent assay (ELISA) kits.

(3) Survival outcomes: Patients were followed monthly after treatment to assess survival. Progression-free survival (PFS) was defined as the time from treatment initiation to disease progression. Overall survival (OS) was defined as the time from treatment initiation to death due to cancer. The follow-up lasted for 1 year.

(4) Safety: Adverse events during treatment were analyzed, including gastrointestinal reactions, fever, leukopenia, and immune-related adverse events (e.g., rash, immune-related pneumonia, immune-related diarrhea).

2.5. Statistical analysis

SPSS 26.0 was used for statistical analysis. Measurement data (mean ± standard deviation) were analyzed using *t*-tests, while categorical data [*n* (%)] were analyzed using χ^2 tests. A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of clinical efficacy between the two groups

The DCR and ORR in the combination group were slightly higher than those in the chemotherapy group, but the differences were not statistically significant ($P > 0.05$). See **Table 1**.

Table 1. Comparison of clinical efficacy between the two groups [*n* (%)]

Group	PD	SD	PR	CR	DCR	ORR
Chemotherapy (*n* = 52)	18 (34.62)	10 (19.23)	22 (42.31)	2 (3.85)	34 (65.38)	17 (32.69)
Combination (*n* = 50)	17 (34.00)	14 (28.00)	19 (38.00)	0 (0.00)	36 (72.00)	19 (38.00)
χ^2					0.518	0.314
P					0.472	0.575

3.2. Comparison of immune-related factor levels between the two groups

Before treatment, there were no significant differences in IFN-γ, IL-2, and VEGF levels between the two groups ($P > 0.05$). After treatment, both groups showed significant increases in IFN-γ and IL-2 levels and significant decreases in VEGF levels ($P < 0.05$). The combination group exhibited superior changes compared to the chemotherapy group ($P < 0.05$). See **Table 2**.

Table 2. Comparison of immune-related factor levels between the two groups (mean ± SD)

Group	IFN-γ (μg/L)		IL-2 (ng/mL)		VEGF (ng/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Chemotherapy (*n* = 52)	1.17 ± 0.19	3.51 ± 0.77*	1.98 ± 0.52	12.33 ± 2.01*	34.97 ± 4.46	18.32 ± 1.89*
Combination (*n* = 50)	1.14 ± 0.33	34.82 ± 4.47*	2.04 ± 0.47	176.44 ± 19.22*	36.02 ± 5.01	9.66 ± 1.71*
t	0.565	49.758	0.611	61.237	1.119	24.236
P	0.573	< 0.001	0.543	< 0.001	0.266	< 0.001

*Note: Comparison within the same group before and after treatment, $P < 0.05$.

3.3. Survival analysis

Follow-up results showed that the PFS and median OS in the chemotherapy group were 5.19 and 10.15 months, respectively, compared to 8.24 and 18.23 months in the combination group. The differences were statistically significant ($P < 0.05$). See **Figure 1**.

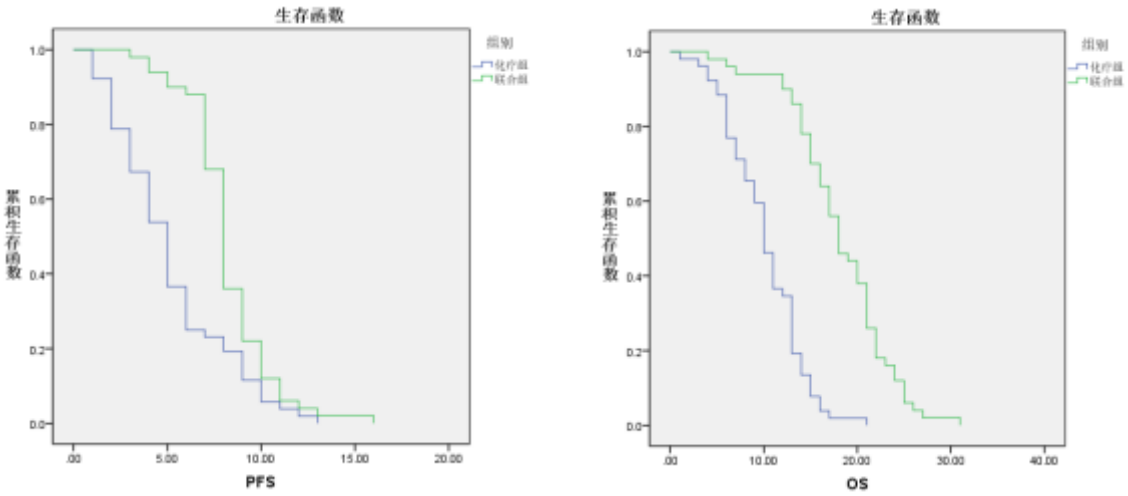

Figure 1. PFS **(left)** and OS **(right)** of patients in the two groups

3.4. Comparison of adverse reaction incidence between the two groups

During treatment, the incidence of rash, immune-related pneumonia, and immune-related diarrhea was higher in the combination group compared to the chemotherapy group ($P < 0.05$). There were no significant differences in the incidence of gastrointestinal reactions, fever, or leukopenia between the two groups ($P > 0.05$). See **Table 3**.

Table 3. Comparison of adverse reaction incidence between the two groups [n (%)]

Group	Gastrointestinal reactions	Fever	Leukopenia	Rash	Immune-related pneumonia	Immune-related diarrhea
Chemotherapy ($n = 52$)	14 (26.92)	22 (42.31)	7 (13.46)	3 (3.85)	1 (1.92)	4 (7.69)
Combination ($n = 50$)	13 (26.00)	19 (38.00)	10 (20.00)	11 (22.00)	8 (16.00)	13 (26.00)
χ^2	0.011	0.197	0.785	5.671	6.279	6.151
P	0.916	0.657	0.376	0.017	0.012	0.013

4. Discussion

Patients with advanced urothelial carcinoma often present with clinical symptoms such as weight loss, fatigue, hematuria, and difficulty urinating, which severely impact their safety and quality of daily life [7]. Various chemotherapy regimens have demonstrated certain clinical efficacy in treating urothelial carcinoma. Among these, the GC chemotherapy regimen has become the first-line treatment due to its high efficacy and relatively low incidence of adverse reactions [8]. Studies using the GC regimen for advanced bladder cancer have shown an objective survival rate of approximately 35% and a median survival time of 14 months [9]. However, despite its efficacy, the long-term survival benefits of the GC regimen remain limited, necessitating further improvements in treatment strategies.

In recent years, immunotherapy has garnered attention for its efficacy in cancer treatment. This approach activates antitumor immunity and reduces tumor immune evasion, offering hope for extending patient survival. Toripalimab, a recombinant humanized anti-PD-1 monoclonal antibody injection, binds with high affinity to PD-1 and selectively blocks the interaction between PD-1 and PD-L1, reactivating T cells and enhancing tumor cytotoxicity. It has been successfully applied in cancers such as liver and gastric cancers, with notable therapeutic effects [10,11].

In this study, the combination group achieved a DCR of 72.00% and an ORR of 38.00%, higher than the chemotherapy group (65.38% and 32.69%, respectively), though the differences were not statistically significant ($P > 0.05$). Additionally, follow-up results revealed that the PFS and median OS in the combination group were 8.24 and 18.23 months, respectively, significantly longer than those in the chemotherapy group ($P < 0.05$). These findings suggest that GC combined with toripalimab effectively improves ORR and extends survival in patients with advanced urothelial carcinoma.

The study also showed that VEGF levels significantly decreased in both groups after treatment, with a more pronounced reduction in the combination group. VEGF is closely associated with tumor angiogenesis and is significantly related to tumor metastasis and progression. These results indicate that toripalimab combined with GC chemotherapy can inhibit tumor neovascularization. Moreover, levels of IFN-γ and IL-2 increased after treatment. This can be attributed to the GC regimen: gemcitabine enhances cisplatin's chemosensitivity

and promotes immunogenic cell death in tumors. The action of the PD-1 inhibitor enhances the recognition and presentation of tumor antigens by dendritic and macrophage cells, leading to increased levels of IFN-γ and IL-2. These changes recruit and activate large numbers of T cells and cytotoxic cells, improving immune function and thus enhancing treatment efficacy and prolonging survival [12].

Regarding safety, patients treated with the combination of toripalimab and chemotherapy experienced higher incidences of rash, immune-related pneumonia, and immune-related diarrhea. However, the incidences of gastrointestinal reactions, fever, and leukopenia were comparable between the two groups. This highlights the need for effective measures to prevent rash, pneumonia, and other adverse events to ensure medication safety during treatment with the combination regimen.

5. Conclusion

In conclusion, the combination of the GC chemotherapy regimen with toripalimab effectively improves clinical outcomes and extends survival in patients with advanced urothelial carcinoma while maintaining acceptable safety. However, attention should be given to preventing adverse reactions such as rash and pneumonia to ensure treatment safety.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Gandhi J, Chen JF, Al-Ahmadie H, 2022, Urothelial Carcinoma: Divergent Differentiation and Morphologic Subtypes. Surg Pathol Clin, 15(4): 641–659. https://doi.org/10.1016/j.path.2022.07.003

[2] Coleman JA, Yip W, Wong NC, et al., 2023, Multicenter Phase II Clinical Trial of Gemcitabine and Cisplatin as Neoadjuvant Chemotherapy for Patients With High-Grade Upper Tract Urothelial Carcinoma. J Clin Oncol, 41(8): 1618–1625. https://doi.org/10.1200/JCO.22.00763

[3] Uccello M, Adeleke S, Moschetta M, et al., 2023, Immunotherapy for Advanced Urothelial Carcinoma (UC): Rational and Current Evidence. Ann Palliat Med, 12(6): 1345–1354. https://doi.org/10.21037/apm-22-1350

[4] 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.

[5] Xu L, Zhang C, Wang D, et al., 2023, Neoadjuvant Immunotherapy Combined with Chemotherapy Followed by Surgical Treatment of Locally Advanced Upper Urinary Tract Urothelial Carcinoma: A Case Report. Practical Oncology Journal, 38(5): 476–480.

[6] Yang X, Wu Y, 2004, RECIST Criteria for Evaluating the Efficacy of Solid Tumor Treatments. Evidence-based Medicine, 4(2): 25–30.

[7] Xiang Y, 2024, Prognostic Significance of Urea and Immune-Inflammatory Markers in Advanced Urothelial Carcinoma Treated with Immunotherapy, dissertation, Jilin University.

[8] Li H, Chen H, Wang L, et al., 2024, Nutritional Risk and Influencing Factors During Chemotherapy in Patients with

Urothelial Carcinoma. Tumor Metabolism and Nutrition Electronic Journal, 11(1): 60–64.

[9] Liu T, 2018, The Impact of Kushen Injection Combined with GC Chemotherapy on Chemotherapy Tolerance and Median Survival in Patients with Advanced Bladder Cancer. Drug Evaluation, 15(9): 35–38.

[10] Wu X, Deng J, Luo T, 2024, Efficacy of Toripalimab Combined with Lenvatinib TACE in the Treatment of Advanced Liver Cancer and Its Impact on Tumor Markers for Prognosis. Hebei Medicine, 30(10): 1745–1751.

[11] Li M, Han M, Li Z, 2023, Clinical Observation of Hepatic Arterial Chemoembolization Combined with Toripalimab in the Treatment of Liver Cancer. Tianjin Pharmacy, 35(3): 53–56.

[12] Xie Q, 2024, Efficacy of Different Chemotherapy Regimens in the Treatment of Advanced Urothelial Carcinoma and Their Impact on Immune Function. Jilin Medical Journal, 45(2): 276–279.