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RESEARCH ARTICLE

Effectiveness and safety of adjuvant treatment of tislelizumab with or without chemotherapy in patients with high-risk upper tract urothelial carcinoma: a retrospective, real-world study

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Abstract

Background Upper tract urothelial carcinoma (UTUC) is a rare subset of urothelial cancers with poor prognosis. No consensus exists on the benefit of adjuvant immunotherapy for patients with UTUCs after nephroureterectomy with curative intent and the existing studies are limited. Herein, this study aimed to evaluate the effectiveness and safety of adjuvant treatment of tislelizumab with or without chemotherapy in patients with high-risk UTUC.

Methods A retrospective study was conducted on 63 patients with high-risk UTUC who received tislelizumab with or without gemcitabine-cisplatin (GC) chemotherapy regimen after surgery between January 2020 and December 2022. Data on demographic and clinical characteristics, surgical, outcomes, prognostic factors, and safety were collected and analyzed.

Results Among the 63 patients with high-risk UTUC, the median age was 66 years (interquartile range 57–72), with 33 (52%) being male. The majority of patients with staged pT3 (44%) and pN0 (78%) disease. Fifty-one patients (81%) received tislelizumab plus GC chemotherapy, and 12 (19%) were treated with tislelizumab monotherapy. After the median follow-up of 26 months (range 1–47), 49 (78%) patients achieved stable disease. The 2-year disease-free survival (DFS) and 2-year overall survival were 78.68% (95% CI: 60.02–87.07%) and 81.40% (95% CI: 68.76–89.31%), respectively. The cycles of GC chemotherapy were independent prognostic factors for survival, with higher DFS (hazard ratio = 0.68, 95% CI, 0.50–0.93; $p = 0.016$) observed in the subgroup undergoing ≥ 3 cycles versus < 3 cycles of GC chemotherapy. Fifty-eight patients (92%) experienced at least one treatment-related adverse event (TRAE), with grade 3–4 TRAEs occurring in 13%. The most common grade 3–4 TRAEs were decreased white blood cells, thrombocytopenia, and ulcers.

Conclusions The study demonstrates promising clinical benefits and a manageable safety profile of the tislelizumab-based adjuvant regimen for patients with high-risk UTUC. This suggests that adjuvant immunotherapy represents a potential therapeutic strategy for this population.

Keywords Upper tract urothelial carcinoma · High-risk · Tislelizumab · Toxicity · Survival

Introduction

Upper tract urothelial carcinoma (UTUC; transitional cell carcinoma of the ureter or renal pelvis) is rare with an estimated annual incidence of approximately 2 cases per 100,000 people and accounts for 5–7% of urothelial carcinomas [1]. Due to scant symptoms and delayed diagnosis, 60% of patients present with invasive disease, and 30% of patients present with metastatic disease at diagnosis [2, 3]. Meanwhile, UTUC has a higher mortality rate compared to other genitourinary tract malignancies [4]. The standard of care for high-risk UTUC is radical nephroureterectomy (RNU, including open, laparoscopic, or robotic approach)

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and excision of the ipsilateral bladder cuff [1]. However, surgical treatment alone is insufficient for individuals with high-risk UTUC because some patients may still experience lethal metastasis and recurrence, and this procedure is associated with a significant postoperative decrease in renal function [5]. Adjuvant chemotherapy has demonstrated great improvement in the prognosis of patients following RNU. The POUT trial, which evaluated the benefit of adjuvant gemcitabine–platinum combination chemotherapy after RNU versus surveillance, reported a significant improvement in disease-free survival (DFS) in patients with locally advanced UTUC [6]. However, a primary potential concern of adjuvant chemotherapy is that renal function may deteriorate after RNU [7]. Therefore, it is crucial to explore new therapeutic options to manage this population and significantly increase their survival rate.

Recently, there has been growing evidence supporting the effectiveness of immune checkpoint inhibitors (ICIs) in the treatment of urothelial carcinoma, leading to the approval of several agents for use as first- and second-line treatment for advanced urothelial carcinoma [8, 9]. Platinum-based chemotherapy can boost the concomitant blocking effects of programmed death 1 (PD-1)/programmed death ligand-1 (PD-L1) while also inducing immune regulatory effects [10]. Based on these synergistic mechanisms, the application of a combination of immunotherapy and chemotherapy has been utilized in various cancers, demonstrating favorable clinical outcomes and manageable safety profiles [11–13]. However, given there is a paucity of data concerning the use of ICI-chemotherapy combinations for patients with high-risk UTUC in adjuvant treatment settings, the survival benefit of the combination of chemotherapy and immunotherapy remains uncertain [4, 6].

Tislelizumab (BeiGene, Co., Ltd., Beijing, China) is a humanized immunoglobulin G4 monoclonal antibody characterized by its high affinity and binding specificity for programmed death-1 (PD-1) [14]. Notably, it can minimize Fcγ receptor binding on macrophages, consequently disrupting the antibody-dependent phagocytosis mechanism associated with T cell clearance and potential resistance to anti-PD-1 therapy [15]. Recent trials evaluating the efficacy of tislelizumab combined with platinum-based (such as gemcitabine plus cisplatin [GC]) chemotherapy had revealed that the combination could increase encouraging antitumor activity with manageable tolerability in patients with advanced non-small cell lung cancer and esophageal squamous cell carcinoma or gastric/gastroesophageal junction adenocarcinoma [16, 17]. However, the existing evidence regarding the use of tislelizumab in conjunction with chemotherapy for high-risk UTUC patients is limited. Thus, we conduct a real-world study to assess the effectiveness and safety of tislelizumab with or without GC chemotherapy in patients with high-risk UTUC.

Materials and methods

Patients and treatment

This was a retrospective analysis of real-world data of 63 patients with high-risk UTUC who were treated with tislelizumab plus GC chemotherapy or tislelizumab monotherapy between January 2020 and December 2022 at Xijing Hospital of Air Force Military Medical University Center (Department of Urology). The inclusion criteria were as follows: (1) eligible patients had pathologically confirmed urothelium carcinoma; (2) patients had preoperative computed tomography (CT) examination and ureteroscopy showing UTUC; (3) patients were stage with T_2-$T_{4a}N_{0-1}$ or T_1N_1 based on the 7th edition of American Joint Committee on Cancer tumor-node-metastasis (TNM) classification; (4) patients had an Eastern Cooperative Oncology Group performance score (ECOG PS) of 0 or 1 and adequate renal function. The exclusion criteria were: (1) patients who had been diagnosed with other tumors within 1 year before their initial diagnosis or who had a concurrent diagnosis of another cancer at the time of initial diagnosis; (2) patients who received neoadjuvant therapy before surgery; (3) PATIENTS who received other immunotherapeutic drugs during adjuvant therapy; (4) patients who lacked follow-up data on glomerular filtration rate (GFR); (5) patients assessed with other disease stages.

The study was done in conformance with the Declaration of Helsinki and local applicable regulatory guidelines. This study was approved by the ethics committee of Xijing Hospital and exempt from informed consent due to its retrospective nature.

Eligible patients underwent surgery (open surgery, laparoscopic nephroureterectomy, or robotic-nephroureterectomy) and adjuvant treatment was initiated within 90 days after surgery. Adjuvant treatment included 21-day cycles of tislelizumab (200 mg administered intravenously on day 1 of each cycle) with or without GC chemotherapy (gemcitabine: 1000 mg/m^2, administered intravenously on days 1 and 8 of each cycle; cisplatin: 70 mg/m^2, administered intravenously on day 2 of each cycle) for 6 cycles. Treatment continued until the disease progressed, intolerable toxicities, or death. The decision on whether patients received GC chemotherapy was based on their clinical realities. Specifically, patients with potential risk factors for cisplatin intolerance did not receive chemotherapy. These factors included a GFR of less than 60 mL/min, grade 2 neuropathy, or grade 2 hearing loss. In addition, some elderly patients or those who refused

GC chemotherapy for subjective reasons were also excluded from receiving this treatment.

Data collection and outcomes

All data was retrospectively collected from medical records, including baseline characteristics, surgical, pathological, systemic treatment, clinical outcomes, and adverse events (AEs). The study outcomes were DFS, overall survival (OS), and safety. DFS was calculated from surgery to the recurrence of primary tumor, last follow-up visit, or death. OS was calculated from the date of the initiation of treatment to death due to any cause or to the last follow-up visit. Radiological evaluation was performed by CT and/or magnetic resonance imaging at the last follow-up visit for disease progression or recurrence, according to Response Evaluation Criteria in Solid Tumors version 1.1 [18]. Treatment-related AEs (TRAEs) and immune-related AEs (irAEs) were defined and graded according to Common Terminology Criteria for Adverse Events version 4.0 by the physician.

Statistical analysis

The patient's demographic and clinical data were analyzed using descriptive statistical analysis. Continuous variables were expressed as medians and ranges or interquartile ranges (IQR). Classification variables were examined using Fisher's exact test for subgroup analysis. DFS and OS were estimated using the Kaplan–Meier method and compared using the log-rank test. The 95% confidence intervals (CIs) for survival curves were calculated using the two-sided Clopper–Pearson method. DFS and OS of subgroups were also investigated according to treatment regimen (tislelizumab combined with GC chemotherapy or tislelizumab monotherapy). In addition, univariable and multivariable Cox proportional hazard models were established to examine the association of clinical variables with DFS and OS. We selected the following factors as variables in univariable Cox regression analysis: age, tumor types, pathological types, history of smoking status, ECOG PS, pathological T stage, N stage, renal function, cycles of tislelizumab, and cycles of GC chemotherapy; and those with a p-value of < 0.2 were then included in multivariate Cox regression analysis. Hazard ratios (HR) with a 95% CI were reported. All significance levels were set at 0.05. The statistical analysis was carried out using SPSS software version 23.0 (SPSS Inc., Chicago, IL, USA).

We had taken various measures to minimize the potential bias and confounding factors. First, relatively strict inclusion and exclusion criteria were established in this study to ensure that all patients included in the study met the requirements. Second, confounding factors were adjusted using the Cox regression model; meanwhile, the clinicopathological factors included in the model were identified from the literature as potentially influencing UTUC prognosis and were validated by internal clinical experts [19, 20]. No excessive confounding factors were included in the multivariate Cox regression analysis, which reduced bias in the study and improved the accuracy of the research results. In the end, owing to the limited sample size of patients enrolled in this study, we adopted a lenient criterion for variable selection, wherein factors with a p value less than 0.2 in the univariate analysis were included in the subsequent multivariate analysis to ensure that potentially relevant variables were not prematurely excluded.

Results

Patient characteristics and treatment

Among the 63 high-risk UTUC patients included in this study, the median age was 66 years (IQR 57–72), with 33 (52%) being male, and half of them had an ECOG performance status of > 1 (52%). The majority of patients staged pT2 and pT3 (pT2, 33%; pT3, 44%) and staged pN0 (78%). Fifty-five (87%) patients had a GFR of 50 mL/min or higher. Detailed clinical characteristics are summarized in Table 1.

Median follow-up was 26 months (range 1–47), with 89% (56/63) of patients being followed up for more than 12 months and 51% (32/63) for more than 24 months. Among 63 patients, after the median duration from surgery to initial adjuvant treatment of 6 weeks (range 3–8), 51 (81%) received tislelizumab plus GC chemotherapy, and 12 (19%) received tislelizumab monotherapy; 48 (76%) were treated with ≥ 3 cycles of tislelizumab; 33 (52%) were treated with ≥ 3 cycles of GC chemotherapy.

Clinical outcomes

As of March 2024, for all 63 patients, 29 (40.03%) achieved stable disease after surgery and continued for 2 years without disease progression or recurrence; 9 developed disease recurrence with a recurrence rate of 14.29%; 13 died (Fig. 1).

The 1-year DFS and 2-year DFS were 82.54% (95% CI: 70.69–89.93%) and 78.68% (95% CI: 60.02–87.07%), respectively. In parallel, the OS at 1-year and 2-year was 87.30% (95% CI: 76.21–93.44%) and 81.40% (95% CI: 68.76–89.31%), respectively (Fig. 2). The median DFS and OS were not reached.

In addition, a subgroup analysis was conducted according to treatment regimen (patients treated with tislelizumab plus GC chemotherapy [$n = 51$] or tislelizumab monotherapy [$n = 12$]). The 2-year DFS in the tislelizumab plus GC chemotherapy group versus the tislelizumab monotherapy

Table 1 Baseline clinical characteristics

Variable	All patients ($n=63$)
Age (median), years	66 (32–84)
<65	27 (43)
≥65	36 (57)
Sex, *n*, %	
Male	33 (52)
Female	30 (48)
History of smoking status, *n*, %	
Yes	19 (30)
No	44 (70)
ECOG performance status, *n*, %	
0–1	30 (48)
2–3	33 (52)
Pathological T stage, *n*, %	
T1	10 (16)
T2	21 (33)
T3	28 (44)
T4	4 (6)
Pathological N stage, *n*, %	
N0	49 (78)
N1	14 (22)
GFR (mL/min)	
30–49	8 (12.70)
≥50	55 (87.30)
Site of tumor, *n*, %	
Renal pelvis	34 (54)
Ureter	24 (30)
Both	5 (8)
Type of surgery, *n*, %	
Open	8 (13)
Laparoscopic	54 (86)
Robotic	1 (2)
GC chemotherapy, *n*, %	
<3 Cycles	30 (48)
≥3 Cycles	33 (52)

ECOG Eastern Cooperative Oncology Group, *GFR* glomerular filtration rate, *GC* cisplatin plus gemcitabine

group was 79.60% and 75.00%, respectively. There was no significant difference in DFS between the two subgroups (HR = 1.22, 95% CI: 0.31–4.72; $p=0.76$; Supplementary Fig. 1A). Similarly, no statistical significance was seen for OS between the two subgroups (HR = 0.65, 95% CI: 0.17–2.43; $p=0.37$), with 2-year OS of 79.30% in the chemotherapy group versus 91.67% in the monotherapy group (Supplementary Fig. 1B).

Univariate and multivariate analyses

To examine the relationship between clinical variables and DFS or OS in high-risk UTUC patients, we performed univariate and multivariable Cox regression analyses (Table 2). Multivariate Cox regression analysis showed nodal stage and cycles of GC chemotherapy (<3 cycles vs. ≥3 cycles) were independent prognostic risk factors for DFS. The cycles of GC chemotherapy had a significant correlation with the benefits of DFS, and ≥3 cycles of GC chemotherapy prolonged DFS versus <3 cycles of GC chemotherapy (HR = 0.68, 95% CI, 0.50–0.93; $p=0.016$; Fig. 3A).

Similarly, the pathological T stage and nodal stage were independent prognostic risk factors for OS. Although a trend in favor of GC chemotherapy ≥3 cycles group in OS was noted, no significant difference was found between GC chemotherapy cycles (HR = 0.78, 95% CI, 0.59–1.08; $p=0.11$; Fig. 3B).

Safety

In terms of safety, a total of 58 (92%) patients experienced at least one TRAE (Table 3). The most frequent TRAEs of any grade included renal injury (41%), hematuria (27%), hepatic injury (24%), urinary tract infection (24%), and decreased white blood cells (19%). Notably, 42 patients exhibited more than one TRAE concurrently. Grade 3–4 TRAEs occurred in 13% of patients, with decreased white blood cells (8%) and thrombocytopenia (3%), as well as ulcers (2%), being the most prevalent. The majority of TRAEs were chemotherapy-related. In addition, 20 patients (32%) experienced irAEs, with the most frequent occurrences (>5%) including renal injury (24%), urinary tract infections (24%), thyroid dysfunction (10%), and abnormal heart function (8%). No grade 3–4 irAEs were observed. Among the 54 patients receiving tislelizumab plus GC, 12 discontinued GC chemotherapy due to TRAEs and were only treated with ≤2 cycles of GC chemotherapy. Thirteen deaths occurred, with one resulting from subsequent hepatobiliary malignancy and the others attributable to disease progression.

Discussion

To date, this is the first real-world retrospective study to explore the effectiveness and safety of adjuvant immunotherapy focusing on high-risk UTUC in China. Our findings show that tislelizumab with or without GC chemotherapy yielded encouraging survival benefits, with 2-year DFS and 2-year OS of 78.68% and 81.40%, respectively. The safety

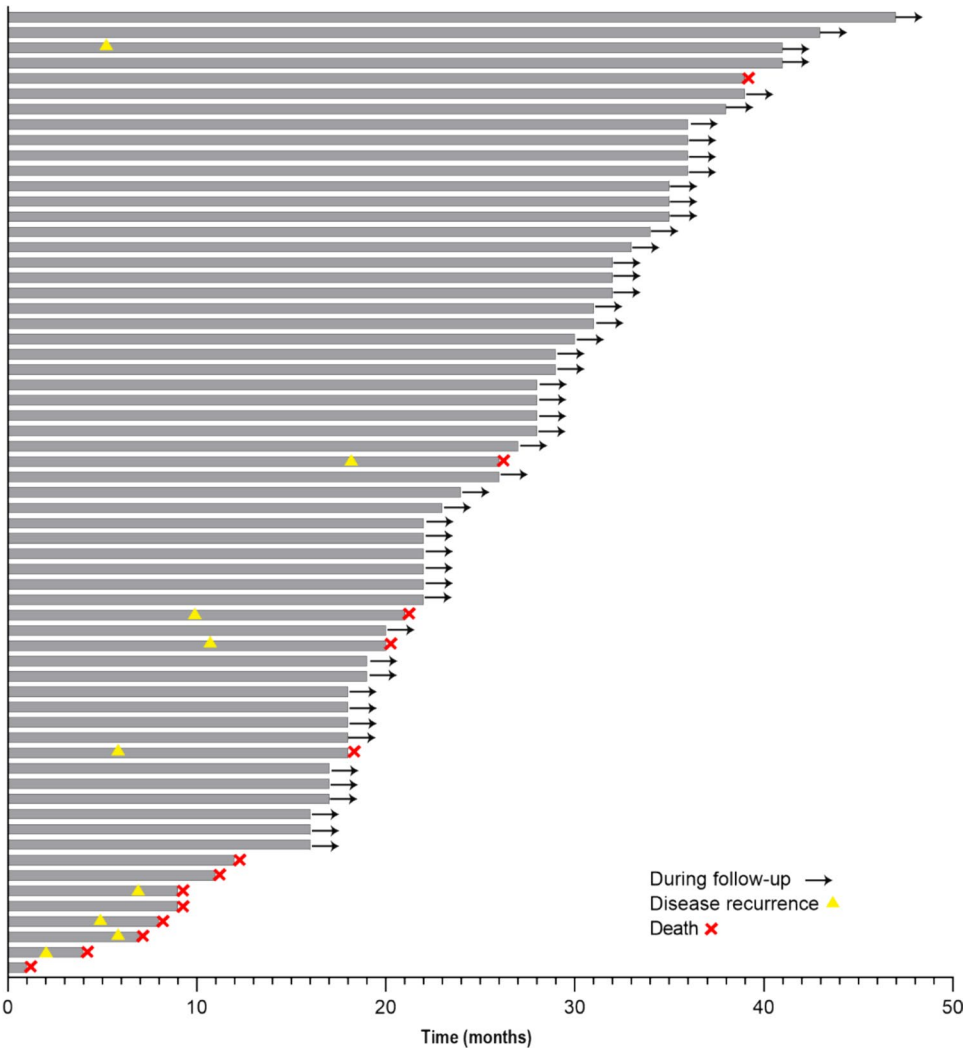

Fig. 1 Swimming plot of treatment exposure and duration of recurrence or death for all population

profile of this regimen was tolerable and manageable. In addition, univariate and multivariate analyses of survival suggested that the cycles of GC chemotherapy were an independent prognostic factor of survival.

It is generally believed that the standard treatment for high-risk UTUC includes RNU and excision of the ipsilateral bladder cuff [8], but the rate of bladder tumor recurrence following RNU remains high, with recurrence events in the bladder occurring in up to 22–47% of the patients within the first postoperative year [21, 22]. The majority of research indicates that postoperative adjuvant chemotherapy can enhance the possibility of survival of patients with UTUC [6, 23]. The phase III POUT trial assessing adjuvant gemcitabine-platinum combined chemotherapy (initiated within 90 days after RNU) with surgery alone demonstrated significant DFS (3-year DFS of 71%) benefit of adjuvant chemotherapy in high-risk nonmetastatic UTUC [6]; Meanwhile, adjuvant chemotherapy conferred a 30% reduction in relative risk of death, with a 3-year OS rate of 79%, but not reaching statistical significance yet [24]. However, the major downside of adjuvant chemotherapy in UTUC is that after RNU, patients often suffer a decline in their renal function, with only about 20% of patients having a postoperative GFR of > 60 mL/min [25]. Consequently, there is a growing interest in exploring alternative adjuvant therapies, such as immunotherapy. The CheckMate 274 trial randomly assigned patients with muscle-invasive urothelial carcinoma to receive 1 year of adjuvant nivolumab or placebo and found a DFS benefit (74.9%) with the addition of adjuvant nivolumab [26]. The IMvigor-010 study evaluated the use of adjuvant atezolizumab in patients with locally advanced or metastatic UTUC who had previously received platinum-based chemotherapy [27]. This was a negative trial with no DFS benefit in the intention-to-treat population. However, there is limited data on the use of adjuvant immunotherapy in the management of UTUC [4].

Based on the excellent therapeutic effects demonstrated by chemotherapy and ICIs, a combination of ICIs and GC chemotherapy is being used clinically for various cancers, including urothelial carcinoma. In our study, we investigated

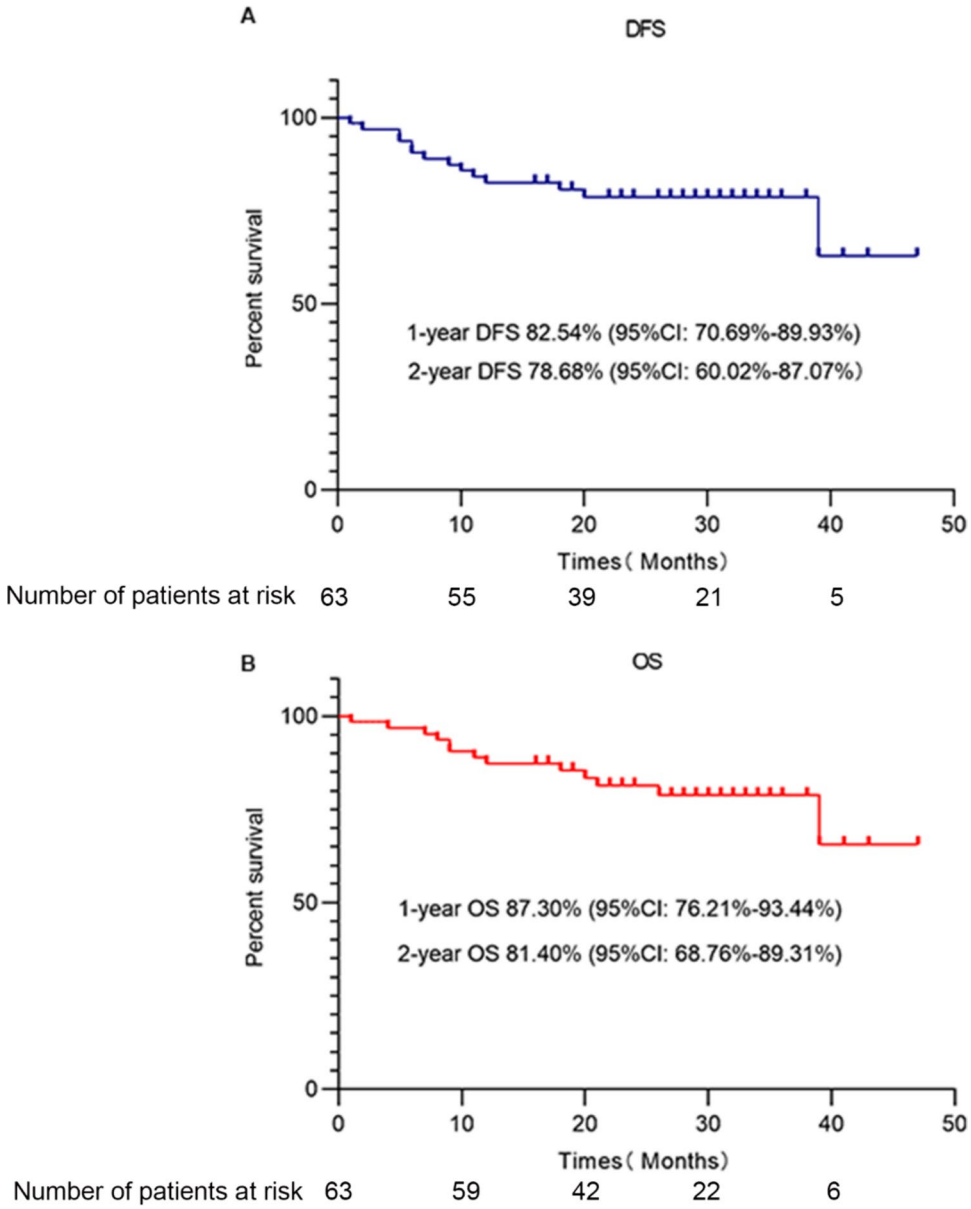

Fig. 2 Survival curves of DFS (**A**) and OS (**B**). *DFS* disease-free survival, *OS* overall survival

the clinical effectiveness and safety of tislelizumab with or without GC as a first-line adjuvant treatment for patients with high-risk UTUC. The patients exhibited a recurrence rate of only 14.29%, lower than the recurrence rates of 22–47% reported in the literature above following RNU [21, 22]. Meanwhile, the results yielded 2-year DFS and 2-year OS of 78.68% and 81.40%, and a clear plateau survival curve had been reached after 2 years. This suggests that our regimen has a low recurrence rate at the 2-year follow-up. Ploussard et al. assessed the OS rates after RNU and showed a 2-year OS of 79.50% [28]. In comparison, our 2-year OS rate (81.40%) is similar; however, given that our patient population exclusively comprises high-risk UTUC, it suggests that our OS outcomes may be more favorable. Overall, this analysis suggests that our tislelizumab-based adjuvant regimen is also a potentially feasible strategy for patients with high-risk UTUC, as it provides an effective survival benefit.

Considering the relatively small sample size of our study and the incomplete understanding of prognostic factors affecting UTUC, we used the probability cutoff of 0.2 to select candidate variables in the univariate analysis and included those with $p < 0.2$ in the multivariable model. The stringent threshold of $p < 0.05$ in univariate analysis may lead to the omission of potentially important factors. By adopting a more lenient p value threshold (such as $p < 0.2$), we aim to minimize the risk of overlooking these factors [29]. In multivariate analysis, $p < 0.05$ is still used as the threshold to ensure the relative objectivity of the results. Multivariate analysis revealed that the T stage and nodal stage serve as independent predictors

Table 2 Univariate and multivariate analyses of DFS and OS

Candidate variables	DFS						OS					
	Univariate			Multivariate			Univariate			Multivariate		
	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*
Age (< 65 vs. ≥ 65 years)	1.027	0.947–1.113	0.519				1.083	0.978–1.200	0.126	1.069	0.987–1.159	0.101
Sex (male vs. female)	0.546	0.126–2.357	0.417				0.804	0.159–4.064	0.792			
Tumor types	0.820	0.221–3.037	0.766				1.872	0.445–7.874	0.393			
Pathological types (low grade vs. high grade)	0.794	0.121–5.216	0.810				0.355	0.064–1.963	0.235			
ECOG PS (< 2 vs. ≥ 2)	1.164	0.382–3.553	0.789				1.345	0.397–4.558	0.634			
History of smoking status (yes vs. no)	0.522	0.084–3.248	0.486				1.287	0.166–10.005	0.809			
T stage (≤ T2 vs. > T2)	3.112	1.057–9.169	0.039	2.208	0.987–4.941	0.054	4.477	1.388–14.446	0.012	4.689	1.727–12.733	0.002
N stage (N0 vs. N1)	10.083	1.652–61.544	0.012	9.402	2.053–43.058	0.004	13.711	1.990–94.473	0.008	13.406	2.742–65.547	0.001
Renal function (GFR ≥ 50 vs. < 50 mL/min)	0.552	0.044–6.936	0.645				0.890	0.071–11.220	0.928			
Tislelizumab cycles (≥ 3 vs. < 3)	1.003	0.848–1.187	0.972				0.900	0.736–1.101	0.307			
GC chemotherapy cycles (≥ 3 vs. < 3)	0.714	0.523–0.974	0.033	0.683	0.500–0.932	0.016	0.802	0.583–1.102	0.174	0.788	0.588–1.057	0.112

for DFS or OS, which align with those reported in our study [30]. Our results also showed that cycles of GC chemotherapy were an independent prognostic factor in survival, with a notably higher survival rate observed in the subgroup undergoing GC chemotherapy for three or more cycles compared to those receiving fewer than three cycles (HR = 0.68, 95% CI, 0.50–0.93; $p = 0.016$). Currently, there is a lack of studies elucidating the relationship between the number of chemotherapy cycles and survival in adjuvant chemotherapy in UTUC. Our study suggests that beyond the impact of whether or not chemotherapy is administered on the survival of UTUC patients [31, 32], the specific number of chemotherapy cycles emerges as a crucial and nuanced factor requiring in-depth exploration. Subsequent randomized controlled trials should be undertaken to further explore the role of chemotherapy cycles in the survival of UTUC patients.

In terms of safety profile, the tislelizumab with or without GC chemotherapy regimen is generally well tolerated and manageable in our study. The TRAEs of any grade in our study was 92.06%, with grade ≥ 3 TRAEs occurring in 12.70%. Notably, the incidence of grade ≥ 3 TRAEs was lower than observed in adjuvant chemotherapy (44%) in the POUT trial [6]. The most common TRAEs included renal injury (41.27%), hematuria (26.98%), hepatic injury (23.81%), urinary tract infection (23.81%), and decreased white blood cells (19.05%). The increased incidence of TRAEs was associated with chemotherapy. The TRAEs observed align with the documented AEs associated with tislelizumab and CG chemotherapy in the studies [33–35], and no unexpected adverse reactions beyond the expectations have been noted. However, nearly all of the patients (except one patient) with treatment failure (recurrence or progression) died in our study. For those who experienced treatment failure, we attempted salvage therapies. For patients who experience recurrence or progression after 12 months post-initial treatment, alternative regimens were considered. These included combinations such as albumin-bound paclitaxel with tislelizumab, disitamab vedotin (an antibody–drug conjugate targeting HER2), or other supportive care measures tailored to the patient's condition. For patients whose recurrence or progression occurred more than 12 months after the initial treatment, if the patient had adequate renal function and no contraindications, re-challenging with tislelizumab plus GC chemotherapy was a preferred option. In addition, regular follow-up with imaging and clinical assessments was conducted to detect recurrence or progression early.

Certain limitations of our study should be acknowledged. First, our study is limited by its retrospective nature; hence, there exists a potential selection bias. Second, the sample size of this study was relatively small. Future studies should include a larger sample size, and

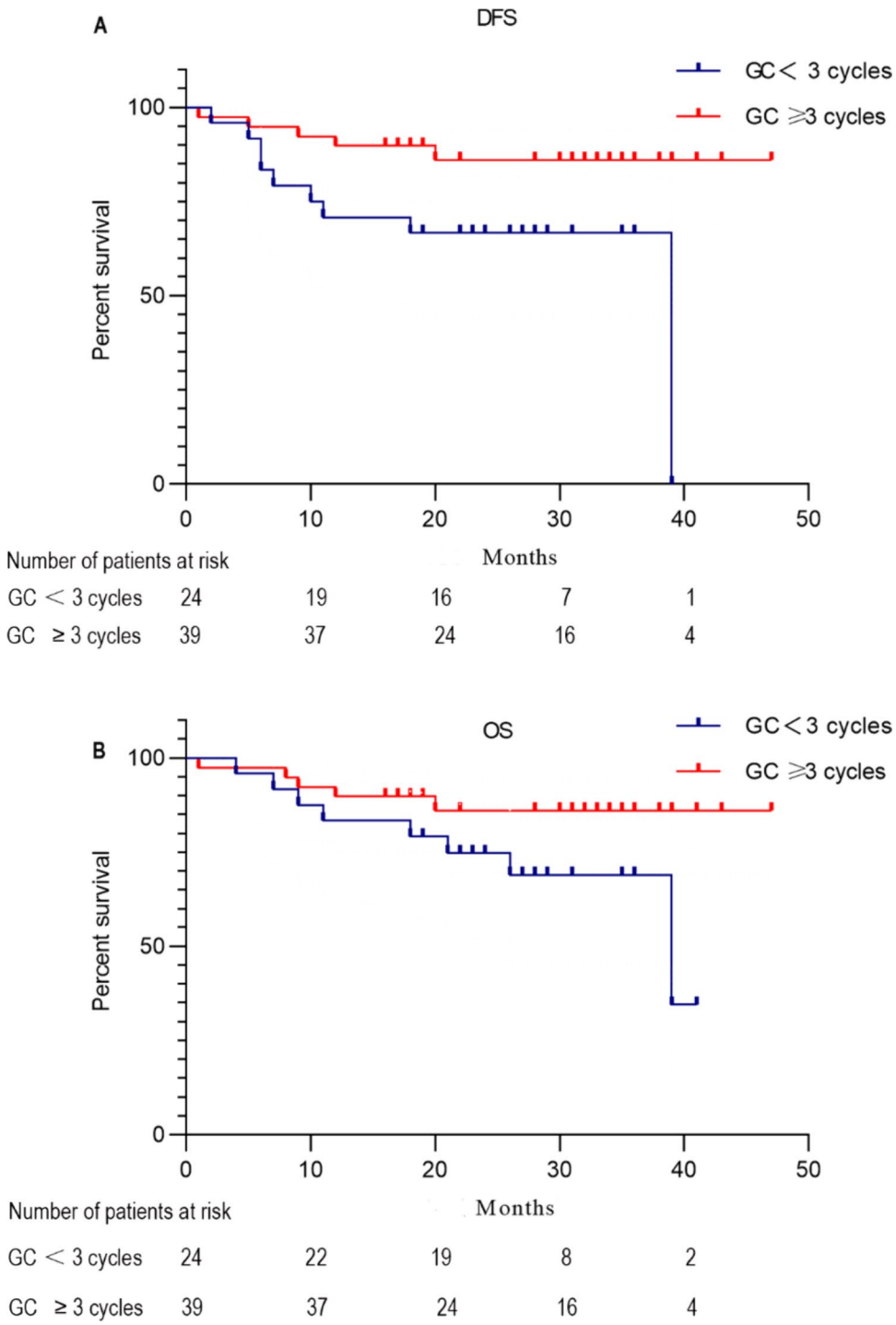

Fig. 3 Survival curves of DFS (**A**) and OS (**B**) patients stratified according to GC chemotherapy (< 3 vs. ≥ 3 cycles). *DFS* disease-free survival, *OS* overall survival

randomized clinical studies should be conducted. Third, there is a lack of long-term follow-up results. Long-term follow-up is needed to understand the long-term prognosis of patients. Fourth, there is an imbalance in the number of patients with tislelizumab plus GC chemotherapy and tislelizumab alone, and related interpretations should be approached with caution.

Conclusion

In summary, the data presented in this retrospective study indicate that the tislelizumab with or without GC chemotherapy regimen, as adjuvant treatment for high-risk UTUC, yields promising effectiveness and a well-tolerated safety profile. These findings suggest that the tislelizumab-based regimen could potentially serve as a viable treatment option

Table 3 Treatment-related adverse events

Performed term	Any grade, *n* (%)	Grade 1–2, *n* (%)	≥ Grade 3, *n* (%)
TRAE			
Renal injury	26 (41)	26 (41)	0
Hematuria	17 (27)	17 (27)	0
Hepatic injury	15 (24)	15 (24)	0
Urinary tract infection	15 (24)	15 (24)	0
Decreased white blood cell	12 (19)	7 (11)	5 (8)
Thyroid dysfunction	6 (10)	6 (10)	0
Abnormal heart function	5 (8)	5 (8)	0
Anemia	3 (5)	3 (5)	0
Rash	3 (5)	3 (5)	0
Thrombocytopenia	2 (3)	0	2 (3)
Ulcer	1 (2)	0	1 (2)
Increased white blood cells	1 (2)	1 (2)	0
irAE			
Renal injury	15 (24)	15 (24)	0
Urinary tract infection	15 (24)	15 (24)	0
Thyroid dysfunction	6 (10)	6 (10)	0
Abnormal heart function	5 (8)	5 (8)	0
Rash	3 (5)	3 (5)	0
Ulcer	1 (2)	1 (2)	0
Increased white blood cells	1 (2)	1 (2)	0

TRAE treatment-related adverse event, *irAE* immune-related adverse event

for high-risk UTUC. Further investigation of the efficacy and safety of the tislelizumab-based regimen for high-risk UTUC through a larger scale randomized controlled study is warranted.

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Data availability The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethics approval and consent to participate This study was approved by the ethical review board of the Xijing Hospital and was conducted under the Declaration of Helsinki and local applicable regulatory guidelines. Since this study was retrospective, there was no informed consent of patients.

Consent for publication Not applicable.

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