Review Article

Advances in chemoablation in upper tract urothelial carcinoma: overview of indications and treatment patterns

Josh Gottlieb[1], Jennifer Linehan[1], Katie S. Murray[2]^

[1]Department of Urologic Oncology, St. John's Cancer Institute, Santa Monica, CA, USA; [2]Department of Urology, NYU Langone Medical Center, New York, NY, USA

Contributions: (I) Conception and design: KS Murray; (II) Administrative support: KS Murray; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: J Gottlieb; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Katie S. Murray, DO, MS, FACS. Department of Urology, NYU Langone Medical Center, 222 E 41st St., New York, NY 10017, USA. Email: Katie.Murray@nyulangone.org.

Abstract: Localized upper tract urothelial carcinoma (UTUC) is a difficult disease for clinicians to treat, due to the multitude of oncological and patient factors to consider. Despite the challenges of diagnostic staging, endoscopic management, and disease recurrence, there is still a need for local therapeutic options that do not subject patients to the morbidities of radical nephroureterectomy (RNU). Intraluminal chemotherapies have allowed for improved oncological control in patients with low-grade disease receiving renal-sparing treatment approaches. This narrative review discusses the treatment modalities available for localized low-grade UTUC, with a focus on the current status of chemoablation. The OLYMPUS trial was a pivotal study that lead to the Food and Drug Administration (FDA) approval of UGN-101 (mitomycin-C) in April 2020 for the treatment of low-grade UTUC, and intraluminal chemotherapy is now a widely used modality for managing this disease. The trial reported a complete response (CR) rate of 59%, and an estimated treatment durability of 82% at 1 year. However, a concern was the reported 44% ureteral stricture rate using the retrograde approach. More research is currently underway to determine the ideal instillation method for intraluminal therapies (e.g., retrograde vs. antegrade). Lastly, we discuss upcoming treatment options. Newer novel agents like padeliporfin vascular targeted photodynamic (VTP) therapy (brand name TOOKAD) are currently being studied, which will in hope provide additional treatment options for UTUC patients.

Keywords: Upper tract urothelial carcinoma (UTUC); UGN-101; chemoablation

Submitted Feb 02, 2023. Accepted for publication Jul 27, 2023. Published online Aug 01, 2023.
doi: 10.21037/tau-23-69
View this article at: https://dx.doi.org/10.21037/tau-23-69

Introduction

Upper tract urothelial carcinoma (UTUC) is a challenging disease to treat for clinicians, as there are many oncological and patient factors to consider. For example, tumor grade, stage, size, focality, and location can all affect treatment decisions. In addition, the patient's baseline renal function, presence of a contralateral kidney, life expectancy, and overall ability to undergo anesthesia also affect clinician management. As a result, the management of UTUC patients is highly variable. The purpose of this review is to highlight current UTUC treatment options, with a focus on recent advances in chemoablation.

Epidemiology

UTUC is a rare urologic malignancy, representing only

^ ORCID: 0000-0002-2633-9438.

5–10% of all urothelial carcinoma (UC), with an estimated annual incidence in Western countries of only 2 new cases per 100,000 person-years (1,2). The disease most commonly affects patients in their 7th–9th decades of life, but the mean age at diagnosis has increased over the last 30 years (3). Compared to UC of the bladder, where 15–25% of patients present with invasive disease, over 30% of UTUC patients will have invasive disease at time of diagnosis (4). With respect to location, pelvicalyceal tumors are diagnosed twice as often as ureteral tumors most likely due to improvements in imaging technology. Gender also plays a significant role in UTUC incidence, where men are 3× more likely to develop UTUC (*vs.* 4× more likely in bladder cancer) (5). However, gender does not usually appear to be associated with survival outcomes except for in endemic areas of the world. A retrospective study in 2019 found that women in Taiwan were more likely to be diagnosed with UTUC, yet had improved overall survival (OS) and cancer-specific survival (CSS) compared to men (6).

The timing of UTUC in relation to bladder UC is also relevant. UC is known to be a multifocal disease with a propensity to recur after treatment. Classically it has been thought that development of UTUC after primary bladder cancer was between 2–7%, yet more recent studies suggest this may actually be as low as 0.8% (7,8). On the contrary, developing bladder cancer after a primary UTUC is reported to be approximately 15–50% (9,10). There are two theories that have been proposed as an explanation for the high rate of bladder recurrences: intraluminal seeding (epithelial migration) and in-field cancerization (2,11). As a result, it is difficult to establish if additional tumor sites are new primary "*de novo*" lesions or seeding sites from the original primary. However, the much higher rates of bladder UC recurrence compared to contralateral upper tract recurrence after upper tract surgery for primary UTUC favors the intraluminal seeding theory. Although not definitively proven, tumor cell seeding with the antegrade flow of urine through the ureters may be related to the higher rates of bladder UC after primary UTUC *vs.* the opposite sequence. Furthermore, an intact ureterovesical junction preventing retrograde flow of tumor cells may also be protective of upper tract recurrence after a primary bladder UC.

To counteract the high rates of bladder recurrence after upper tract surgery, postoperative intravesical chemotherapy has been shown to reduce bladder recurrence rates. The ODMIT-C (12) trial was a prospective trial consisting of 284 patients with no previous or concurrent history of bladder UC undergoing radical nephroureterectomy (RNU) for suspected UTUC. Patients received 40 mg of mitomycin-C upon removal of the urinary catheter, which led to an absolute reduction in risk of intravesical recurrence of 11% (12). Similarly, the SWOG S0337 trial was another prospective study consisting of 383 patients with suspected low-grade non-muscle-invasive bladder UC. This study found that immediate postresection intravesical instillation of gemcitabine, compared with instillation of saline, significantly reduced the risk of recurrence over a median of 4.0 years (13).

Diagnosis

Two-thirds of patients with UTUC present with either gross or microscopic hematuria, and 25% will present with flank pain related to ureteral or renal obstruction from the upper tract tumor (2). Rarely, UTUC will be detected incidentally on imaging [computed tomography (CT) or magnetic resonance imaging (MRI)]. Constitutional symptoms such as weight loss, anorexia, fever, malaise, night sweats, and cough are suspicious for advanced or metastatic disease.

Initial workup should involve a detailed history that assesses for UTUC risk factors and a physical exam. Initial laboratory tests consist of microscopic urinalysis, urine culture, urine cytology, and blood tests to assess for renal function and hemoglobin. Other urinary markers like fluorescence in situ hybridization (FISH), nuclear matrix protein 22 (NMP-22), and other biomarkers are still preliminary and their role in UTUC diagnosis remains unclear (1). Imaging is obtained using CT/MRI urography, renal ultrasound, or retrograde pyelography. After obtaining initial lab tests and imaging, patients will typically undergo cystoscopy and ureteroscopy where a biopsy can then be performed.

Treatment options

In primary bladder cancer, the depth of tumor involvement or T stage guides management. However, accurate pathological staging is rarely feasible for UTUC given the current technological limitations and anatomical challenges (i.e., small ureteral lumen and thin layer of smooth muscle) in determining muscle involvement. As a result, the disease grade predominantly dictates management decisions.

For high-grade, bulky, or invasive localized disease, RNU with ipsilateral bladder cuff excision has remained the gold-

standard treatment. Minimally invasive *vs.* open approaches to RNU have created some level of controversy. The European Association of Urology (EAU) guidelines still recommend either technique depending on the skill level of the surgeon, but the surgery must include a negative margin resection and lymph node dissection (14). The National Comprehensive Cancer Network (NCCN) guidelines version 1.2023 for UTUC do not make any statement in regard to surgical approach for RNU (15). Patients with low-grade disease but high in volume, determined by either imaging or visual inspection, have also undergone RNU. As diagnostic techniques improve, those with low-grade/low-risk localized disease have the potential of being treated with kidney-sparing approaches such as endoscopic ablation, percutaneous resection, intraluminal therapies, and rarely segmental ureterectomy.

Endoscopic ablation

For low-risk UTUC (typically <2 cm, unifocal, low-grade, noninvasive), endoscopic laser ablation via ureteroscopy is recommended with the goal of obtaining complete tumor ablation while preserving renal function. However, a significant challenge with ablative methods is the high rate of local tumor recurrence that may eventually still lead to RNU (16-18). Some studies have quoted >50% risk of progression to RNU in patients with low-grade disease (19). Despite the kidney-sparing potential in low-risk UTUC, <20% of low-grade UTUC was managed endoscopically according to a 2019 National Cancer Database study (20). One of the main hypotheses for this is due to the difficulty in determining low-risk *vs.* high-risk UTUC patients. Some researchers have even proposed an algorithm to help clinicians determine the best candidates for endoscopic ablation (21). Based on the SEER database, patients with low-grade disease who underwent watchful waiting had a disease-free survival of 83%, which makes RNU for low-grade disease appear to be aggressive management (22). A large retrospective analysis in 2014 reported no significant difference in OS and CSS between RNU and endoscopic ablation in 1,002 patients with localized UTUC. Yet they also stated that the findings should be interpreted with caution due to the low level of evidence (3b) and heterogeneity among the studies (23). Another systematic review from 2016 found that only patients with low-grade and noninvasive tumors experienced similar CSS after ureteroscopy or percutaneous management when compared to RNU, despite an increased risk of local UTUC recurrence (24). Similar to the prior mentioned study, they recommend caution when interpreting the results due to selection bias favoring kidney-sparing surgery. A more recent technology that has provided some respite for surgeons is the thulium laser fiber. This enables tissue ablation with more efficient hemostatic control aiding in both diagnosis and treatment (25). Ureteroscopic baskets and biopsy forceps can also be used for mechanical ablation, however, presenting the extensive data surrounding all of the different endoscopic techniques is not the primary focus of this review.

Intraluminal therapies

Intraluminal therapies are typically given after endoscopic ablation or resection, and consist of Bacille Calmette-Guerin (BCG) or cytotoxic chemotherapy (e.g., mitomycin-C or gemcitabine). The NCCN UTUC guidelines version 1.2023 states that intraluminal therapies can be given as a treatment following endoscopic ablation of low-grade tumors in the renal pelvis and ureter (15). These agents can be given via three routes: (I) retrograde via ureteral catheter; (II) retrograde via passive reflux from an indwelling ureteral stent; or (III) antegrade via nephrostomy tube. Currently, there is no literature to suggest improved oncologic outcomes with one method compared to another.

BCG

The role for BCG in the upper tracts is usually limited to carcinoma in situ (CIS), yet the current NCCN guidelines still list it as an option for post-surgical instillation following endoscopic resection in low-grade tumors of the renal pelvis. A retrospective analysis from 2011 found that the efficacy of BCG for treating CIS in the upper tracts (risk of recurrence: 40%, progression: 5%) is similar to its efficacy for bladder CIS (26). However, for Ta/T1 lesions the efficacy was lower (risk of recurrence: 59%, progression 41%) compared to the equivalent bladder stage. Thus, BCG is not commonly used for non-CIS UTUC.

Intraluminal chemotherapy

One of the main challenges with intraluminal instillation is the rapid drainage of instilled fluid from an unobstructed collecting system. As a result, there is limited dwell time between the therapeutic agent and the tumor. In order to address this problem, Urogen Pharmaceuticals created

Jelmyto™, also known as UGN-101, which gained Food and Drug Administration (FDA) approval in April 2020 for the treatment of low-grade UTUC based on the results of the OLYMPUS trial. UGN-101 is a reverse thermosensitive hydrogel polymer containing mitomycin-C that exists as a liquid in cold temperatures and quickly changes to a gel at body temperature. This agent gradually dissolves in urine over 4–6 hours, and allows for slow release of mitomycin-C with increased dwell time within the collecting system.

The OLYMPUS trial was a phase 3, multicenter, single-arm prospective clinical trial that included patients with at least 1 measurable low-grade papillary tumor ≤1.5 cm and no suspicion for high-grade disease (27). Only tumors in the renal pelvis or calyces were eligible for treatment. Although typically given as an adjuvant therapy following endoscopic ablation or resection, this study was able to assess the chemoablation ability of UGN-101 because there was known existing disease at time of treatment. Patients received 6 weekly retrograde instillations of UGN-101, and subsequently underwent ureteroscopic evaluation with urine cytology and for-cause biopsies 4–6 weeks after the last instillation was given. The primary endpoint was complete response (CR) (28) at first evaluation (defined as a negative 3-month ureteroscopic evaluation with negative urine cytology) and showed a CR rate of 59% (27) with 11% of patients obtaining partial response (PR). Of the 42 patients (59%) that obtained a CR, only 6 had a recurrence. A subset of patients with CR at first evaluation (n=20) were assessed for treatment durability by undergoing monthly maintenance treatments with evaluations at 6, 9, and 12 months. CR durability was estimated to be 82% at 12 months follow-up based on Kaplan-Meier analysis. Interestingly, CR durability at 1 year was similar between those that had ≥1 maintenance doses (6/12 patients; 50%) and those that did not (17/29 patients; 59%) (29). In regard to adverse events, the most common were ureteral strictures (44%), urinary tract infection (32%), hematuria (31%), flank pain (30%), and nausea (24%). More than 40% of patients experienced a ≥ grade 3 adverse event. The ureteral stricture rate also appeared to be related to number of doses, however, statistical analysis was not performed for this observation. Ureteral stricture was reported in 19/29 patients (66%) who received ≥7 instillations of UGN-101 (i.e., induction course plus ≥1 maintenance instillations) compared to 12/42 patients (29%) who received only an induction course (6 instillations of UGN-101).

Instillation methods

As previously mentioned, intraluminal UGN-101 can be given via retrograde or antegrade approaches and the prior data available was with retrograde instillation. Traditionally urologists have been cautioned against percutaneous biopsy, percutaneous management, or even placement of a nephrostomy tube in the setting of UTUC, but several studies have shown these procedures to be safe (30,31). Earlier this year, Rosen *et al.* published their method for antegrade instillation with early outcomes on their first 8 patients (32). These patients received instillation in the clinic via nephrostomy tube, which had the advantages of foregoing additional trips to the operating room with general anesthesia. Four patients had a CR (28), and four patients had a PR. Although it is difficult to make conclusions on oncologic outcomes from a small case series with short-term follow-up, they described an easily reproducible technique and protocol to instill UGN-101.

Treatment approach also needs to consider adverse events in addition to oncologic outcomes. Perhaps the main concerns from the adverse events listed in the OLYMPUS trial is the ureteral stricture rate of 44%. Currently there is no published data comparing ureteral stricture rates between antegrade and retrograde approaches, however, this data will likely become available soon as antegrade instillations become increasingly common.

Upcoming treatments

Unlike prostate cancer, there are less treatment modalities available for UTUC. Although endoscopic ablation and intraluminal instillations have remained the most commonly used modalities, new treatments are currently under investigation. The ENLIGHTED Trial is a phase 3, single arm, non-randomized, multicenter trial evaluating the safety and efficacy of padeliporfin (brand name TOOKAD) vascular targeted photodynamic (VTP) therapy in the treatment of low-grade UTUC. Once activated, padeliporfin triggers the production of high levels of radical oxygen species, which cause destruction of the blood vessels supplying the tumor followed by rapid death of tumor cells (31). Padeliporfin VTP will be given intravenously at 3.66 mg/kg with subsequent ureteroscopy. During ureteroscopy, an optical light fiber will be passed through the ureteroscope and illuminate the target area for 10 minutes. The primary endpoint will be CR rates. Secondary endpoints will assess

for treatment durability, renal function preservation, adverse events, etc. The trial has an estimated primary completion date of February 2024, but the study completion date is projected to be in 2029 (33).

Conclusions

Although rare, UTUC is a challenging malignancy to treat due to the heterogeneous nature of the disease. As such, clinicians need to be versatile in their ability to utilize multiple treatment strategies. Intraluminal chemotherapies have allowed for improved oncological control in patients with low-grade disease receiving renal-sparing treatment approaches. More research is currently underway to determine the ideal instillation method for intraluminal therapies. Newer novel agents (e.g., TOOKAD) are also being studied, which will in hope provide additional treatment options for UTUC patients.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editors (Ram A. Pathak and Ashok K. Hemal) for the series "Upper Tract Urothelial Cancer" published in *Translational Andrology and Urology*. The article has undergone external peer review.

Peer Review File: Available at https://tau.amegroups.com/article/view/10.21037/tau-23-69/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-23-69/coif). The series "Upper Tract Urothelial Cancer" was commissioned by the editorial office without any funding or sponsorship. JL is a consultant and speaker bureau for Urogen Pharmaceuticals, Inc. KSM is a consultant and speaker bureau for Urogen Pharmaceuticals, Inc and a president for Missouri Urological Association. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Białek Ł, Bilski K, Dobruch J, et al. Non-Invasive Biomarkers in the Diagnosis of Upper Urinary Tract Urothelial Carcinoma-A Systematic Review. Cancers (Basel) 2022;14:1520.
2. Petros FG. Epidemiology, clinical presentation, and evaluation of upper-tract urothelial carcinoma. Transl Androl Urol 2020;9:1794-8.
3. Raman JD, Messer J, Sielatycki JA, et al. Incidence and survival of patients with carcinoma of the ureter and renal pelvis in the USA, 1973-2005. BJU Int 2011;107:1059-64.
4. Del Giudice F, van Uem S, Li S, et al. Contemporary Trends of Systemic Neoadjuvant and Adjuvant Intravesical Chemotherapy in Patients With Upper Tract Urothelial Carcinomas Undergoing Minimally Invasive or Open Radical Nephroureterectomy: Analysis of US Claims on Perioperative Outcomes and Health Care Costs. Clin Genitourin Cancer 2022;20:198.e1-9.
5. Shariat SF, Favaretto RL, Gupta A, et al. Gender differences in radical nephroureterectomy for upper tract urothelial carcinoma. World J Urol 2011;29:481-6.
6. Huang CC, Su YL, Luo HL, et al. Gender Is a Significant Prognostic Factor for Upper Tract Urothelial Carcinoma: A Large Hospital-Based Cancer Registry Study in an Endemic Area. Front Oncol 2019;9:157.
7. Sanderson KM, Cai J, Miranda G, et al. Upper tract urothelial recurrence following radical cystectomy for transitional cell carcinoma of the bladder: an analysis of 1,069 patients with 10-year followup. J Urol 2007;177:2088-94.
8. Wright JL, Hotaling J, Porter MP. Predictors of upper tract urothelial cell carcinoma after primary bladder cancer: a population based analysis. J Urol 2009;181:1035-9; discussion 1039.
9. Azémar MD, Comperat E, Richard F, et al. Bladder

recurrence after surgery for upper urinary tract urothelial cell carcinoma: frequency, risk factors, and surveillance. Urol Oncol 2011;29:130-6.
10. Picozzi S, Ricci C, Gaeta M, et al. Upper urinary tract recurrence following radical cystectomy for bladder cancer: a meta-analysis on 13,185 patients. J Urol 2012;188:2046-54.
11. Mertens LS, Sharma V, Matin SF, et al. Bladder Recurrence Following Upper Tract Surgery for Urothelial Carcinoma: A Contemporary Review of Risk Factors and Management Strategies. Eur Urol Open Sci 2023;49:60-6.
12. O'Brien T, Ray E, Singh R, et al. Prevention of bladder tumours after nephroureterectomy for primary upper urinary tract urothelial carcinoma: a prospective, multicentre, randomised clinical trial of a single postoperative intravesical dose of mitomycin C (the ODMIT-C Trial). Eur Urol 2011;60:703-10.
13. Messing EM, Tangen CM, Lerner SP, et al. Effect of Intravesical Instillation of Gemcitabine vs Saline Immediately Following Resection of Suspected Low-Grade Non-Muscle-Invasive Bladder Cancer on Tumor Recurrence: SWOG S0337 Randomized Clinical Trial. JAMA 2018;319:1880-8.
14. Rouprêt M, Babjuk M, Burger M, et al. European Association of Urology Guidelines on Upper Urinary Tract Urothelial Carcinoma: 2020 Update. Eur Urol 2021;79:62-79.
15. National Comprehensive Cancer Network. Upper GU Tract Tumors (Version 1.2023). Accessed March 30, 2023. Available online: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf
16. Cutress ML, Stewart GD, Wells-Cole S, et al. Long-term endoscopic management of upper tract urothelial carcinoma: 20-year single-centre experience. BJU Int 2012;110:1608-17.
17. Cutress ML, Stewart GD, Zakikhani P, et al. Ureteroscopic and percutaneous management of upper tract urothelial carcinoma (UTUC): systematic review. BJU Int 2012;110:614-28.
18. Fero KE, Shan Y, Lec PM, et al. Treatment Patterns, Outcomes, and Costs Associated With Localized Upper Tract Urothelial Carcinoma. JNCI Cancer Spectr 2021;5:pkab085.
19. Mohapatra A, Strope SA, Liu N, et al. Importance of long-term follow-up after endoscopic management for upper tract urothelial carcinoma and factors leading to surgical management. Int Urol Nephrol 2020;52:1465-9.
20. Upfill-Brown A, Lenis AT, Faiena I, et al. Treatment utilization and overall survival in patients receiving radical nephroureterectomy versus endoscopic management for upper tract urothelial carcinoma: evaluation of updated treatment guidelines. World J Urol 2019;37:1157-64.
21. Petros FG, Li R, Matin SF. Endoscopic Approaches to Upper Tract Urothelial Carcinoma. Urol Clin North Am 2018;45:267-86.
22. Syed JS, Nguyen KA, Suarez-Sarmiento A, et al. Survival outcomes for patients with localised upper tract urothelial carcinoma managed with non-definitive treatment. BJU Int 2018;121:124-9.
23. Yakoubi R, Colin P, Seisen T, et al. Radical nephroureterectomy versus endoscopic procedures for the treatment of localised upper tract urothelial carcinoma: a meta-analysis and a systematic review of current evidence from comparative studies. Eur J Surg Oncol 2014;40:1629-34.
24. Seisen T, Peyronnet B, Dominguez-Escrig JL, et al. Oncologic Outcomes of Kidney-sparing Surgery Versus Radical Nephroureterectomy for Upper Tract Urothelial Carcinoma: A Systematic Review by the EAU Non-muscle Invasive Bladder Cancer Guidelines Panel. Eur Urol 2016;70:1052-68.
25. Proietti S, Johnston T, Pupulin M, et al. Effectiveness and Safety of Thulium Fiber Laser in the Conservative Management of Patients with Upper Tract Urothelial Carcinoma. Eur Urol Open Sci 2022;46:99-104.
26. Giannarini G, Kessler TM, Birkhäuser FD, et al. Antegrade perfusion with bacillus Calmette-Guérin in patients with non-muscle-invasive urothelial carcinoma of the upper urinary tract: who may benefit? Eur Urol 2011;60:955-60.
27. Kleinmann N, Matin SF, Pierorazio PM, et al. Primary chemoablation of low-grade upper tract urothelial carcinoma using UGN-101, a mitomycin-containing reverse thermal gel (OLYMPUS): an open-label, single-arm, phase 3 trial. Lancet Oncol 2020;21:776-85.
28. Bianchi L, Nini A, Bianchi M, et al. The Role of Prostate-specific Antigen Persistence After Radical Prostatectomy for the Prediction of Clinical Progression and Cancer-specific Mortality in Node-positive Prostate Cancer Patients. Eur Urol 2016;69:1142-8.
29. Matin SF, Pierorazio PM, Kleinmann N, et al. Durability of Response to Primary Chemoablation of Low-Grade Upper Tract Urothelial Carcinoma Using UGN-101, a Mitomycin-Containing Reverse Thermal Gel: OLYMPUS Trial Final Report. J Urol 2022;207:779-88.
30. Huang SY, Ahrar K, Gupta S, et al. Safety and diagnostic

accuracy of percutaneous biopsy in upper tract urothelial carcinoma. BJU Int 2015;115:625-32.
31. Joseph JP, Potretzke TA, Packiam V, et al. Percutaneous Image-guided Core Needle Biopsy for Upper Tract Urothelial Carcinoma. Urology 2020;135:95-100.
32. Rosen GH, Nallani A, Muzzey C, et al. Antegrade Instillation of UGN-101 (Mitomycin for Pyelocalyceal Solution) for Low-Grade Upper Tract Urothelial Carcinoma: Initial Clinical Experience. J Urol 2022;207:1302-11.
33. ENdoluminal LIGHT ActivatED Treatment of Upper Tract Urothelial Cancer (ENLIGHTED) Study (UCM301). Accessed April 19, 2023. Available online: https://clinicaltrials.gov/ct2/show/NCT04620239

Cite this article as: Gottlieb J, Linehan J, Murray KS. Advances in chemoablation in upper tract urothelial carcinoma: overview of indications and treatment patterns. Transl Androl Urol 2023;12(9):1449-1455. doi: 10.21037/tau-23-69

