REVIEWS IN UROLOGY

Integrating JELMYTO (Mitomycin) for Pyelocalyceal Solution Into Community Practice: Practical Tips for the Urologist

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Abstract

Treatment options for upper-tract urothelial carcinoma are based on whether the patient has high-risk or low-risk disease. Low-grade tumors can be managed with nephron-sparing approaches, including ureteroscopic resection and ablation, although most patients undergoing endoscopic treatment of upper-tract urothelial cancers face a risk of recurrence. Mitomycin gel for pyelocalyceal solution provides an effective alternative therapy. In OLYMPUS, a phase 3, single-arm, open-label study, 58% of patients with low-grade disease experienced a complete response to induction therapy at 3 months. Kaplan-Meier analysis revealed an estimated 12-month durable response rate of 82%. The most common treatment-emergent adverse events were ureteric stenosis, urinary tract infection, hematuria, and flank pain (grade <3). Mitomycin gel offers a novel, kidney-sparing, nonoperative approach to managing low-grade upper-tract urothelial carcinoma.

Urothelial tumors of the upper urinary tract (upper-tract urothelial carcinoma [UTUC]) pose a unique challenge to practicing urologists. Renal pelvic and ureteral tumors are relatively uncommon, accounting for only 10% of renal tumors and about 5% of all urothelial tumors.[1] Treatment options have historically been limited and are driven by the characterization of high-risk or low-risk disease.[2] High-grade tumors are typically treated with radical nephroureterectomy with or without chemotherapy; however, low-grade tumors can be managed with nephron-sparing approaches, including ureteroscopic resection and ablation. Unfortunately, there is recurrence in the majority of patients undergoing endoscopic treatment of upper-tract urothelial cancers, and the most common approach to managing low-grade UTUC remains radical nephroureterectomy.[3] Given the adverse impact on kidney function resulting from extirpative surgery in patients with low-grade UTUC, improved tools for kidney preservation are sorely needed.

Current Need for Alternatives to Surgical Intervention

Available options for drug therapy in the primary or adjuvant management of low-grade UTUC have been scarce. BCG and mitomycin C have been the most widely investigated adjuvant therapies used with endoscopic resection. The technical limitations of upper-tract accessibility for drug instillation and therapeutic

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exposure have limited the adoption of these agents in the treatment of UTUC. Thus, there is a clear unmet need to develop alternative therapies to treat low-grade UTUC. As barriers to new technology in urology are broken and new realms of possible treatment are explored, the integration of mitomycin for pyelocalyceal solution (Jelmyto; UroGen Pharma) as a robust treatment option for UTUC provides a novel and effective alternative to surgical therapy.

Background of Mitomycin Gel in the Treatment of UTUC

Since the US Food and Drug Administration's 2020 approval of JELMYTO (mitomycin gel) for the treatment of low-grade UTUC in adults, the incorporation of mitomycin gel into treatment regimens has fundamentally changed the management of this type of cancer. With its unique formulation of mitomycin C impregnated into a reverse-thermal gel (RTGel; UroGen Pharma), mitomycin gel provides durable, sustained contact between chemotherapy and the urothelial lining, promoting chemoablation of the urothelial tumor. Mitomycin gel is liquid when chilled and converts to a gel at body temperature within several minutes of entering the body. Over 4 to 6 hours, the medication provides sustained drug delivery; then, the gel dissolves and is excreted through normal urinary function.

The application and use of mitomycin gel were illustrated in the OLYMPUS trial, which led to the agent's Food and Drug Administration approval.[4] OLYMPUS was a phase 3, single-arm, open-label study designed to determine the safety, efficacy, and tolerability of mitomycin gel for the treatment of low-grade UTUC. At 3 months, 58% of patients in the trial experienced a complete response to induction therapy; Kaplan-Meier analysis revealed an estimated 12-month durability of maintaining a complete response of 82%. The most common treatment-emergent adverse events were ureteric stenosis, urinary tract infection, hematuria, and flank pain (few reports of flank pain were rated as grade ≥3). The OLYMPUS trial was the first prospective trial to demonstrate a complete and durable chemoablative response in the treatment of low-grade UTUC.[5]

ABBREVIATION

UTUC upper-tract urothelial carcinoma

Incorporating Mitomycin Gel Into Clinical Practice

Integrating use of mitomycin gel into practice is straightforward. Once an eligible patient with low-grade UTUC is identified and enrolled using the UroGen online patient enrollment form, a clinical team will arrive at the practice location to help initiate care with the agent. Mitomycin gel can be administered in the office, ambulatory surgical center, hospital outpatient department, or in the hospital. The treatment regimen consists of 6 weekly administrations via a retrograde ureteral catheter or percutaneous nephrostomy tube. National Comprehensive Cancer Network guidelines recommend complete or near-complete resection or ablation, but mitomycin gel is effective even if the tumor is unreachable by laser; in fact, almost half the patients in the OLYMPUS trial were deemed to have unresectable tumors.

The instillation volume for mitomycin gel is equal to the patient's renal pelvis and calyceal volume, and instillation is performed by measuring the volume in an antegrade and retrograde fashion via contrast instillation. After 3 measurements of the volume of the upper-tract collecting system, the average volume measured or 15 mL (whichever is lower) is used as the instillation volume. Instillation can be performed at the time of the first mitomycin gel treatment, during nephrostomy tube placement, or even at the time of the initial ureteroscopy. Preparation of the drug consists of initially placing the vial in an ice bath for at least 10 minutes but no longer than 1 hour. When the vial is removed from the ice bath, the clinician has 4 minutes to draw the mitomycin gel into the administration syringe before it solidifies. The syringe is then connected to the URO-Jet applicator (Healthfirst). The agent is instilled by turning the URO-Jet applicator

knob until the entire syringe is emptied. The full process from removing the vial from the ice bath to emptying the syringe completely typically takes about 1 minute.

Primary administrative concerns voiced by urologists we spoke to regarding incorporating mitomycin gel into practice included medication costs, coverage, and reimbursement. Thus, practices must determine whether adding mitomycin gel is feasible from an operational and economic perspective. Some practices initially enter into a partnership with local hospital systems, which then assume the initial risk for reimbursement of the drug. Most practices, after they have gained experience using mitomycin gel, are likely to offer treatments in the office (antegrade instillation) or in an ambulatory surgical center or hospital outpatient department. Although most initial treatments were administered in a retrograde fashion (as described in OLYMPUS), in our practices, the majority of clinicians have adopted antegrade administration via a percutaneous nephrostomy tube in the office. This approach avoids the need for cystoscopy and retrograde ureteral catheter placement once a week for 6 weeks (often with anesthesia) and allows for treatment within a typical 15-minute office visit.

Because of the ease of preparation and use of mitomycin gel, clinicians can be comfortable administering the agent, and training for administration is straightforward for staff. No mixing or hood preparation is required because the medication is delivered from a specialty pharmacy on the day of treatment. We have identified patients eligible for treatment through both referrals and our own navigation program for patients with newly diagnosed and preexisting low-grade UTUC. The incorporation of mitomycin gel into our practice has enabled us to avoid nephroureterectomy in the vast majority of patients with low-grade disease, even those with unresectable tumors.

References

1. Zganjar AJ, Thiel DD, Lyon TD. Diagnosis, workup, and risk stratification of upper tract urothelial carcinoma. *Transl Androl Urol.* 2023;12(9):1456-1468. doi:10.21037/tau-23-45
2. European Association of Urology. EAU guidelines on upper urinary tract urothelial cell carcinoma. 5. Diagnosis. European Association of Urology. Accessed December 18, 2022. https://uroweb.org/guidelines/upper-urinary-tract-urothelial-cell-carcinoma/chapter/diagnosis
3. Verges DP, Lallas CD, Hubosky SG, et al. Endoscopic treatment of upper tract urothelial carcinoma. *Curr Urol Rep.* 2017;18(4):31. doi:10.1007/s11934-017-0675-x
4. 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(6):776-785. doi:10.1016/S1470-2045(20)30147-9
5. 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(4):779-788. doi:10.1097/JU.0000000000002350

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