Medical Information Request: JELMYTO® (mitomycin) for pyelocalyceal solution.

Thank you for your question regarding treatment of ureteral tumors associated with upper tract urothelial carcinoma (UTUC) and JELMYTO.

JELMYTO® is indicated for the treatment of adult patients with low-grade Upper Tract Urothelial Cancer (LG-UTUC). The most common adverse reactions (≥ 20%) are ureteric obstruction, flank pain, urinary tract infection, hematuria, renal dysfunction, nausea, abdominal pain, fatigue, dysuria, and vomiting. Warning and precautions as listed in the FDA Package Insert attached include ureteric obstruction, bone marrow suppression, and embryo-fetal toxicity. Jelmyto® is contraindicated in patients with perforation of the bladder or upper urinary tract. It is recommended to avoid use of JELMYTO in patients with a Glomerular Filtration Rate of < 30 mL/min.[1]

Patients in the pivotal **OLYMPUS trial** had one or more low-grade lesions above the ureteropelvic junction, measuring (by direct visualization at ureteroscopy) 5–15 mm in greatest dimension. 58% (41/71; 95% CI 45-69) of patients achieved complete response (CR) at 3 months, and 56% (23/41; 95% CI 40-72) of patients remained in CR at 12 months.[2] **No patients with ureteral tumors were treated with JELMYTO in the pivotal OLYMPUS phase 3 trial.** However, data for ureteral tumors is available from other studies.

Kleinmann et al. (2019) published "Thermo Reversible Hydrogel Based Delivery of Mitomycin C (UGN-101) for Treatment of Upper Tract Urothelial Carcinoma (UTUC)." In *Bladder Cancer*.[3] This is a retrospective cohort study examining compassionate use of JELMYTO (UGN-101) in 22 patients presenting with UTUC. Patients with ureteral tumor were included, but the study did not specify demographics or provide sub-analysis of results.[3]

The following information presented is from independent retrospective studies. These are independent publications, and no funding was provided by UroGen Pharma.

Woldu et al. (2023) published "Early experience with UGN-101 for the treatment of upper tract urothelial cancer - A multicenter evaluation of practice patterns and outcomes." in *Urologic Oncology* and presented during SUO 2022.[4]

Study Design:

- This is an independent, retrospective review of 132 UTUC patients (136 renal units) treated with JELMYTO with a focus on practice patterns, efficacy, and adverse effects.
- Points of observation include tumor characteristics (i.e. **location; ureter vs renal pelvis vs both**), treatment characteristics, as well as safety and efficacy.
    - Of 136 renal units, 47 cases had tumor involvement of the ureter, with 12 cases below the ureteropelvic junction (UPJ) only (8.8%), and 35 cases both above and below UPJ (26%)
- Treatment method included induction with JELMYTO using six weekly instillations via antegrade or retrograde routes. Post-induction maintenance treatment was used per physician discretion.
- **The following studies are a sub-analysis by Jacob et al. (2024) and a long-term follow up by Woldu et al. (2025) based on this patient cohort.**

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Jacob et al. (2024) published "First analysis of the safety and efficacy of UGN-101 in the treatment of ureteral tumors." in *Urologic Oncology*.[5] This is an independent, retrospective sub-analysis based on the Woldu 2023 cohort, specifically analyzing the treatment of ureteral tumors with JELMYTO.

Study Design:

- This is an independent, retrospective sub-analysis of patients treated with UGN-101 for UTUC and is based on the Woldu 2023 cohort.
- This study is the first to specifically analyze the treatment of ureteral tumors with JELMYTO.
    - 47 cases had tumor involvement of the ureter (34.6%), with 12 cases of ureteral tumors only (8.8%) and 35 cases of ureteral plus renal pelvic tumors (25.7%).
- Patients who received UGN-101 for incompletely treated residual disease were considered to have received chemo-ablative intent treatment, while patients who received UGN-101 for completely ablated disease were considered to have received adjuvant treatment.
    - Of the 47 cases of ureteral tumors, 17 had completely ablated ureteral disease prior to UGN-101 induction and a further 7 patients did not have a follow-up endoscopy – therefore **there were 23 patients evaluable for complete response**.
    - Patients with ureteral tumors were more likely to have multifocal disease (p<0.001), have prior attempts at endoscopic ablation or intracavitary therapy (80.4% vs 61.8%, p=0.03), and less likely to receive antegrade instillation (28% vs 51%, P=0.03) vs patients without ureteral tumor.

Results:

- 23 patients received chemo-ablative intent UGN-101 for ureteral tumors (± pyelocaliceal tumors) with follow-up endoscopy – **complete response rate (CR) in the ureter was 47.8% (n = 11),** 26.1% (n = 6) had a partial response (PR), and another 26.1% (n = 6) had no response (NR).
    - CR was defined as absence of visible disease; PR was defined as decreased tumor burden; and NR was defined as either stability or increase in tumor burden, as estimated by the physician.
- **Results are presented in Table 1 below.**

Table 1: Results from Jacob et al. (2024) study[5]

Endpoints for Ureteral +/- Pyelocaliceal	Patient Results (n=23)		
Response Rate (ureteral +/- pyelocaliceal tumors)	47.8% (n=11) CR	26.1% (n=6) PR	26.1% (n=6) NR
KM Recurrence-Free Survival (adjuvant intent or CR after chemo-ablative intent)	87% at 12 months		
KM Progression-Free Survival (presumed low-grade, non-invasive ureteral UTUC)	78% at 12 months		
Ureteral Stenosis	Ureteral Pts (n=37)	Pyelocaliceal Pts (n=78)	P-value
Pre-existing hydronephrosis	25.5% (n=12)	12.4% (n=11)	*P=0.011*
Post-therapy significant ureteral stenosis	37.8% (n=14)	16.5% (n=13)	*P=0.011*
New onset stenosis (excluding pre-existing hydronephrosis and/or ureteral stenosis)	5.4% (n=2)	2.6% (n=2)	*P=0.429*

KM, Kaplan Meier; CR, complete response; UTUC, upper tract urothelial cancer; PR, partial response; NR, no response or improvement; Pts, patients

Limitations:

This is a retrospective review and its sub-analyses are independent and not funded by UroGen Pharma. Due to the retrospective nature, limitations exist including but not limited to lack of centralized pathology review, short follow up time, and clinically significant ureteral stenosis definition differed from the registration OLYMPUS trial.

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Woldu et al. (2025) published "Durability of response of UGN-101: Longitudinal follow up of multicenter study." in *Urologic Oncology*.[6] This long-term follow up of the Woldu 2023 cohort focused on three-year longitudinal outcomes.

Study Design:

- This is an independent, retrospective long-term follow up study of patients treated with UGN-101 for UTUC and is based on the Woldu 2023 cohort.
- This study presents **three-year**, longitudinal outcomes in the 56 renal units who presented no evidence of disease following JELMYTO induction.
    - 22 cases presented with tumor involvement of the ureter (39.3%), with 8 cases of ureteral tumors only (14.3%) and 14 cases of ureteral plus pelvicalyceal tumors (25%).
- Endpoints included recurrence-free survival (RFS); progression data; and Kaplan Meier survival analysis stratified by relevant clinical features, including tumor location. Median follow-up was 23.5 months.

Results:

- **Results are presented in Table 2 below.**
    - Overall, **65% of renal units were recurrence-free.** Median time to recurrence was not reached, but mean survival estimate was 29.0 months.
- **There was no significant difference in RFS when stratified by tumor location: Ureteral (95% CI 26.6-33.8) vs pelvicalyceal (95% CI 18.8-28.0) vs ureteral + pelvicalyceal (95% CI 18.9-27.5) (P=0.65).**

Table 2: Results from Woldu et al. (2025) study[6]

Endpoints	Results, Renal Units (n=56)			
Overall Recurrence-Free Survival (RFS)	65%; Median time to recurrence not reached; Mean survival estimate 29.0 mo			
RFS Stratified Subgroup Analysis	Estimate of Mean Survival			P-Value
Tumor Location	U, 23.4 mo (n=8)	UP, 23.2 mo (n=22)	P, 30.2 mo (n=14)	*P=0.65*

RFS, recurrence-free survival; Mo, months; U, ureteral; UP, ureteral + pelvicalyceal; P, pelvicalyceal

Limitations:

This is a retrospective review and its sub-analyses are independent and not funded by UroGen Pharma. Due to the retrospective nature, limitations exist including but not limited to lack of centralized pathology review, short follow up time, and clinically significant ureteral stenosis definition differed from the registration OLYMPUS trial.

Please refer to the package insert and www.jelmyto.com for the full Prescribing Information.

As described in the JELMYTO® (mitomycin for pyelocalyceal solution) Prescribing Information:

• INDICATIONS AND USAGE: JELMYTO is an alkylating drug indicated for the treatment of adult patients with low-grade Upper Tract Urothelial Cancer (LG-UTUC).

• ADVERSE REACTIONS: The most common adverse reactions (≥ 20%) are ureteric obstruction, flank pain, urinary tract infection, hematuria, renal dysfunction, nausea, abdominal pain, fatigue, dysuria, and vomiting. Please refer to the attachments for additional Important Safety Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit http://www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to UroGen Pharma at 1-855-987-6436.

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References:

1. Jelmyto® (mitomycin) for pyelocalyceal solution. Prescribing Information 2024. UroGen Pharma, Princeton, New Jersey.
2. 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 Jun;21(6):776-785. doi: 10.1016/S1470-2045(20)30147-9. Epub 2020 Apr 29. https://pubmed.ncbi.nlm.nih.gov/32631491/
3. Kleinmann N, Wirth G, Lin J, et al. Thermo Reversible Hydrogel Based Delivery of Mitomycin C (UGN-101) for Treatment of Upper Tract Urothelial Carcinoma (UTUC). *Bladder Cancer*. 2019 Jan:5(1):21 – 29. DOI: 10.3233/BLC-180182. https://content.iospress.com/articles/bladder-cancer/blc180182
4. Woldu SL, Labbate C, Murray KS, et al. Early experience with UGN-101 for the treatment of upper tract urothelial cancer - A multicenter evaluation of practice patterns and outcomes. *Urol Oncol*. 2023;41(3):147.e15-147.e21. doi:10.1016/j.urolonc.2022.10.029. https://pubmed.ncbi.nlm.nih.gov/36424224/
5. Jacob JM, Woldu SL, Linehan J, et al. First analysis of the safety and efficacy of UGN-101 in the treatment of ureteral tumors. *Urol Oncol*. 2024 Jan;42(1):20.e17-20.e23. doi: 10.1016/j.urolonc.2023.07.004. Epub 2023 Jul 28. https://pubmed.ncbi.nlm.nih.gov/37517898/
6. Woldu SL, Igel D, Johnson B, et al. Durability of response of UGN-101: Longitudinal follow up of multicenter study. *Urol Oncol*. 2025 Jan 20:S1078-1439(24)01059-7. doi: 10.1016/j.urolonc.2024.12.279. Epub ahead of print. https://pubmed.ncbi.nlm.nih.gov/39837708/

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