IN LOW-GRADE UPPER TRACT UROTHELIAL CANCER (LG-UTUC)

ANTEGRADE INSTILLATION OF

Jelmyto®
(mitomycin) for pyelocalyceal solution

An overview of clinical considerations and real-world study experience from multiple practice sites

Indications and Usage

JELMYTO® (mitomycin) for pyelocalyceal solution is indicated for the treatment of adult patients with low-grade Upper Tract Urothelial Cancer (LG-UTUC).

Important Safety Information

Contraindications

JELMYTO is contraindicated in patients with perforation of the bladder or upper urinary tract.

Please see Important Safety Information on page 9 and click here for Full Prescribing Information, Instructions for Pharmacy, and Instructions for Administration. Please click here for INSTRUCTION GUIDE for instillation of JELMYTO® (mitomycin) for pyelocalyceal solution with a nephrostomy tube.

JELMYTO: CLINICAL OVERVIEW

INDICATIONS AND USAGE

JELMYTO® (mitomycin) for pyelocalyceal solution is indicated for the treatment of adult patients with low-grade Upper Tract Urothelial Cancer (LG-UTUC).

DOSING AND ADMINISTRATION[1]

JELMYTO is for pyelocalyceal use only. General anesthesia, local anesthesia, sedation, prophylactic antibiotics, and/or antihistamines may be used at the discretion of the treating urologist.

- Instilled once weekly for 6 weeks, via nephrostomy tube or ureteral catheter
- JELMYTO dose is 4 mg per mL, with total instillation volume based on volumetric measurements using pyelography, not to exceed 15 mL (60 mg of mitomycin)

CLINICAL TRIAL[1,2]

JELMYTO was studied in OLYMPUS, a phase 3, open-label, single-arm, multicenter trial (N=71) in patients with treatment-naïve or recurrent noninvasive LG-UTUC with ≥ 1 measurable papillary tumor 5 to ≤ 15 mm above the ureteropelvic junction (partial tumor resection/debulking was permitted if > 15 mm).

EFFICACY[1,2]

Major efficacy endpoints were complete response (CR) and durability of response.

JELMYTO achieved:

- 58% CR (95% CI: 45, 69)

At the 12-month assessment of durability (n=41):

- 23 (56%) patients remained in CR
- 8 patients had disease recurrence
- 10 patients were inevaluable
  - Median duration of response was not reached, with a range of 0-18.8+ months.

SAFETY[1]

- Serious adverse reactions occurred in 39% of patients who received JELMYTO. Serious adverse reactions in > 3% of patients included ureteric obstruction (including ureteric stenosis and hydronephrosis), flank pain, and urosepsis. Two deaths occurred due to cerebrovascular accident and failure to thrive
- Ureteric obstruction events were reported in 58% of patients, which included ureteric stenosis in 44% of patients. Most events were grade 1 or 2

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THE FLEXIBILITY TO CHOOSE AN ANTEGRADE APPROACH

Antegrade and retrograde instillation are FDA-approved methods of administration for JELMYTO.[1] However, you may find antegrade instillation to be appropriate for your patients and your practice. If you are considering antegrade instillation via nephrostomy tube for your patients, the following information can help facilitate physician-patient decision-making.

FEATURES OF ANTEGRADE ADMINISTRATION[1,3,4]

Logistics for nephrostomy tube	• One-time visit for tube placement after initial biopsy and before first JELMYTO instillation • No fluoroscopy after placement of nephrostomy tube is confirmed by nephrostogram • One-time visit for removal of tube after treatment
JELMYTO instillations	• Anesthesia not needed for instillations • Can be performed in a clinic with the urologist or trained nurses
Patient considerations	• Potential to lessen repeated instrumentation of the upper tract • Nephrostomy tube remains in place throughout the treatment course

CONSIDER ADMINISTRATION VIA NEPHROSTOMY TUBE WHEN[3,4]

Patients prefer an alternate approach

Patients cannot tolerate anesthesia

Practices cannot accommodate weekly fluoroscopy or administration of anesthesia

Antegrade administration was a common instillation method reported in a large, real-world study. Please speak with your UroGen® representative for further information or to access the publication.

OVERVIEW OF AN ANTEGRADE INSTILLATION PROCESS WITH JELMYTO[3]

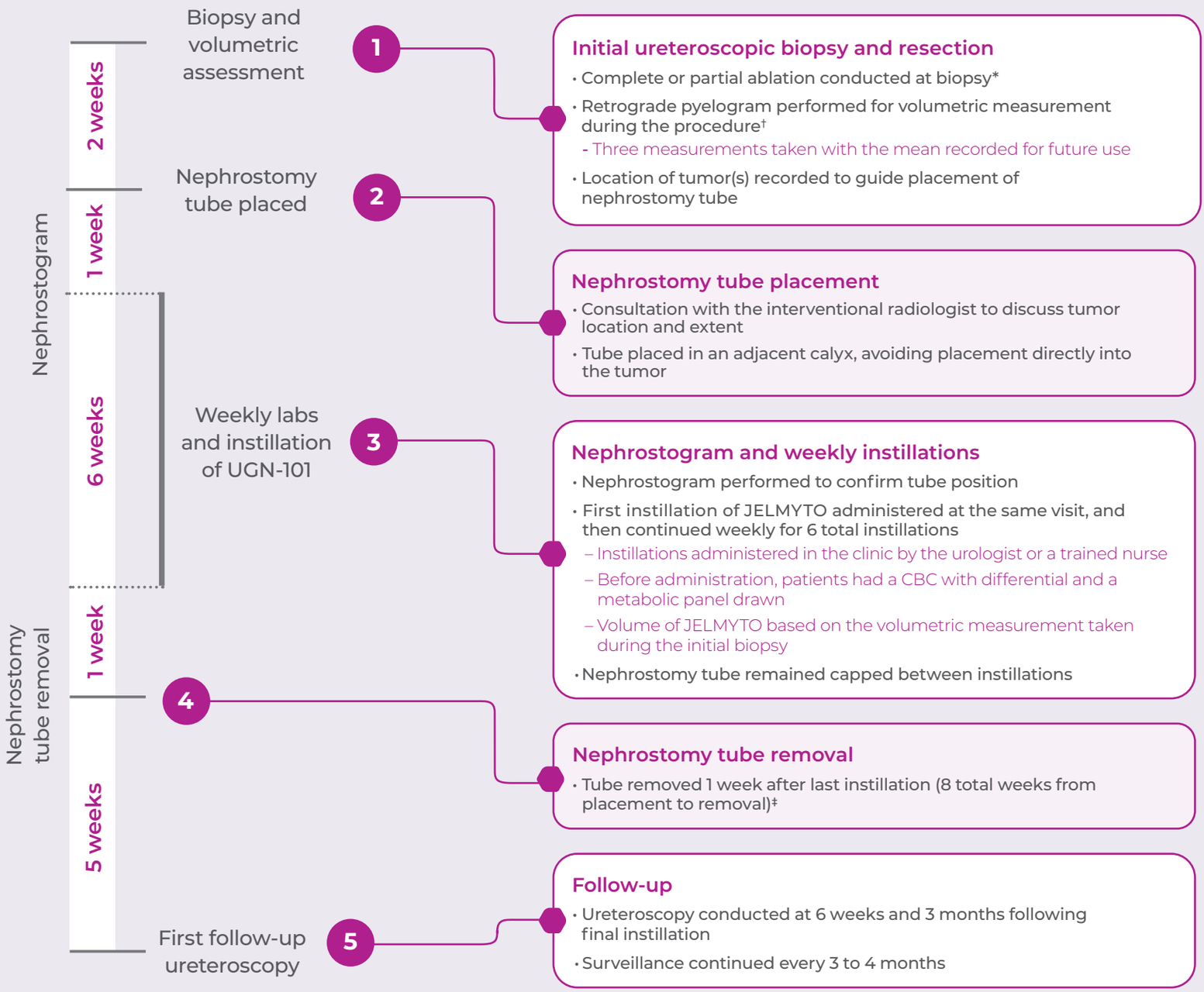
REAL-WORLD CLINICAL EXPERIENCE FROM THE UNIVERSITY OF MISSOURI HEALTH CARE (UMHC)

ROSEN ET AL 2022 STUDY

- Retrospective review of 8 patients with biopsy-proven LG-UTUC treated with JELMYTO at the University of Missouri Health Care
- **Primary objective:** Report on the methods of instilling JELMYTO via antegrade administration through nephrostomy tube
- **Secondary objectives:** Report clinical outcomes, including response and adverse events

Access an antegrade instillation procedural checklist from the article supplement

UMHC PROTOCOL FROM DIAGNOSIS TO FOLLOW-UP[3]



The information portrayed here is specific to the protocol and objectives noted in Rosen et al. While the JELMYTO Prescribing Information allows for antegrade administration, it is important to note that no investigators in the OLYMPUS trial utilized a nephrostomy tube as the mode of administration.

Please note that the protocol used here is specific to the UMHC. Nephrostomy protocols may differ across institutions.

CBC = complete blood count.

*In the OLYMPUS Study, all patients had papillary tumors measuring 5 to ≤ 15 mm prior to retrograde administration of JELMYTO.

†Measurement can also be taken with antegrade pyelogram dependent on institution.

‡If patient is eligible to receive maintenance therapy, the nephrostomy tube can be left in for the duration as long as patient can tolerate.

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REAL-WORLD EVIDENCE: ANTEGRADE ADMINISTRATION IN PRACTICE[4]

The safety and feasibility of antegrade administration of JELMYTO was investigated in an independent, real-world study that evaluated a diverse range of patient presentations

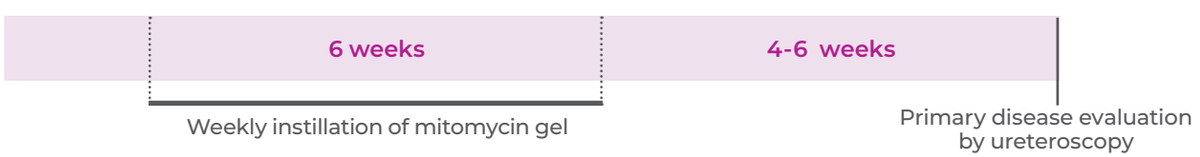
ROSE ET AL 2022 STUDY

- Multi-institutional retrospective review of patients with UTUC undergoing antegrade administration of JELMYTO in 4 tertiary referral centers (N=32)
- **Primary outcome:** Safety, with adverse events captured retrospectively through medical record review
- **Secondary outcomes:** Treatment response and disease recurrence

REAL-WORLD POPULATION: KEY BASELINE CHARACTERISTICS

Median age	74.5 years	**Location**	
Primary tumor	47%	Upper pole	25%
Recurrent tumor	53%	Interpolar	3%
Resectable	75%	Lower pole	19%
Unresectable	25%	Renal pelvis	6%
Median size of largest tumor (IQR)	2 cm (1-3)	Ureter	3%
Solitary kidney	22%	Multifocal	44%

Weekly instillation via percutaneous nephrostomy tube (PCNT)



- Instillations performed in an outpatient clinical setting without anesthesia
- PCNTs remained in place for a median of 8 weeks from initial placement to treatment completion

ADVERSE EVENTS REPORTED IN ROSE ET AL (N=32)[4]

	Grade 1-2 n (%)	Grade 3 n (%)
Fatigue	7 (22%)	0
Flank pain	6 (19%)	0
Ureteric stenosis*	2 (6%)	1 (3%)
Urinary tract infection	1 (3%)	2 (6%)
Infundibular stenosis	2 (6%)	0
Abdominal pain	2 (6%)	0
Anemia	2 (6%)	0
Sepsis	0	2 (6%)
Hematuria	1 (3%)	0
Dysuria	1 (3%)	0
Rash	1 (3%)	0

- The median (IQR) follow-up in the safety cohort was 15.0 (11.8-19.0) months after first dose

*The definition of ureteric stenosis varies across studies. In Rose et al, ureteric stenosis was defined by a discrete narrowing of the ureter on direct visual ureteroscopy, or a constriction identified on retrograde pyelogram at the time of ureteroscopy, that required dilatation or stenting to pass a ureteroscope for upstream visualization. In the OLYMPUS Study, ureteric stenosis was observed in 44% of patients, and overall ureteric obstruction was observed in 58% of patients. This included incidents of hydronephrosis, obstructive uropathy, pelvi-ureteric obstruction, ureteric stenosis, and urinary tract obstruction.[1,4]

PRIMARY DISEASE EVALUATION IN PATIENTS WHO COMPLETED INDUCTION THERAPY (n=29)[4†]

- 59% (n=17) had no evidence of disease
- 38% (n=12) had evidence of tumor at primary disease evaluation
  - 11 of these patients showed a decreased but detectable tumor burden
  - 1 patient demonstrated no change in tumor burden (this patient's tumor was upgraded to high grade, resulting in the need for RNU)
- No recurrence reported at a median follow-up of 13 months (IQR 9-15) in patients with no evidence of disease at evaluation

†Primary disease evaluation was performed at a median of 47 days (IQR 37.5-69) after the last dose of JELMYTO.

Study limitations according to authors

Limitations to the study include its retrospective nature and sample size. The complications and adverse event profile of the antegrade administration of JELMYTO were contingent on patient reporting, and thus may have been underreported. While the multi-institutional nature of the study may support generalizability of the safety profile, varying practice patterns and pathologic analysis may have contributed to confounding. Similarly, the tertiary urologic oncology centers administering JELMYTO percutaneously may have missed adverse events if patients presented to outside institutions for complications. Compared to the OLYMPUS Study, in which the safety analysis group contained 71 patients, this study is smaller in that it only includes the findings from 4 tertiary institutions that were administering JELMYTO through the antegrade method. Larger-scale clinical trials are needed to inform clinical decision-making concerning patients with UTUC.[4]

IQR = interquartile range; RNU = radical nephroureterectomy.

Please see the reported uses of JELMYTO in Rose et al on the following page

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IMPORTANT INFORMATION REGARDING NEPHROSTOMY TUBE MATERIALS AND HEALING TIME PRIOR TO JELMYTO INSTILLATION

Follow practice/institutional protocol regarding placement of the nephrostomy tube as well as the time allowance for healing before proceeding with JELMYTO instillation. Also follow nephrostomy tube removal protocol following treatment course.

- A percutaneous nephrostomy tube (not nephroureteral stent) with molded Luer Lock connector and locking loop must be placed prior to instillation of JELMYTO. Latex catheters or nephrostomy tubes made of latex should not be used during JELMYTO administration due to the risk of deformation attributed with pressure changes, which can impede flow of the hydrogel admixture

For full instructions on how to instill JELMYTO via nephrostomy tube, including how to measure kidney volume prior to instillation, please refer to the *Instruction Guide for Instillation of JELMYTO® (mitomycin) for pyelocalyceal solution With a Nephrostomy Tube,* which can be found on **Jelmyto.com/hcp** or by scanning the QR code on the back cover.

References: 1. JELMYTO [package insert]. Princeton, NJ: UroGen Pharma, Inc.; 2022. **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;21(6):776-785. **3.** Rosen GH, Nallani A, Muzzey C, Murray KS. Antegrade instillation of UGN-101 (mitomycin for pyelocalyceal solution) for low-grade upper tract urothelial carcinoma: initial clinical experience. *J Urol*. 2022;207(6):1302-1311. **4.** Rose KM, Narang G, Rosen G, et al. Antegrade administration of mitomycin gel for upper tract urothelial carcinoma via percutaneous nephrostomy tube: a multi-institutional retrospective cohort study. *BJU Int*. 2023;131(4):471-476.

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Ureteric Obstruction

Ureteric obstruction, including ureteral stenosis and hydronephrosis, occurred in patients receiving JELMYTO. Monitor patients for signs and symptoms of ureteric obstruction, including flank pain, and fever, and for changes in renal function. Patients who experience obstruction may require transient or long-term ureteral stents or alternative procedures. Withhold or permanently discontinue JELMYTO based on the severity of ureteric obstruction.

Bone Marrow Suppression

The use of JELMYTO can result in bone marrow suppression, particularly thrombocytopenia and neutropenia. The following tests should be obtained prior to each treatment: Platelet count, white blood cell count differential and hemoglobin. Withhold JELMYTO for Grade 2 thrombocytopenia or neutropenia. Permanently discontinue for Grade 3 or greater thrombocytopenia or neutropenia.

Embryo-Fetal Toxicity

Based on findings in animals and mechanism of action, JELMYTO can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of mitomycin resulted in teratogenicity. Advise females of reproductive potential to use effective contraception during treatment with JELMYTO and for 6 months following the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with JELMYTO and for 3 months following the last dose.

Common Adverse Reactions

The most common adverse reactions in ≥ 20% of patients treated with JELMYTO were ureteric obstruction, flank pain, urinary tract infection, hematuria, abdominal pain, fatigue, renal dysfunction, nausea, dysuria, and vomiting.

Additional Adverse Reactions Information

Selected clinically relevant adverse reactions in < 10% and ≥ 2% of patients who received JELMYTO include urinary tract inflammation, bladder spasm, urosepsis, hypersensitivity, and instillation site pain.

Use in Specific Populations

Lactation

Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with JELMYTO and for 1 week following the last dose.

Preparation and Administration Information

JELMYTO is for pyelocalyceal use only and not for intravenous use, topical use, or oral administration. JELMYTO must be prepared and administered by a healthcare provider. To ensure proper dosing, it is important to follow the preparation instructions found in the JELMYTO Instructions for Pharmacy and administration instructions found in the JELMYTO Instructions for Administration.

JELMYTO may discolor urine to a violet to blue color following the instillation procedure. Advise patients to avoid contact with urine for at least six hours post-instillation, to void urine sitting on a toilet, and to flush the toilet several times after use.

JELMYTO is a hazardous drug. Follow applicable special handling and disposal procedures.

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FOR ADULT PATIENTS WITH LOW-GRADE UPPER TRACT UROTHELIAL CANCER (LG-UTUC)

ANTEGRADE INSTILLATION OFFERS THE FLEXIBILITY OF AN ADDITIONAL ADMINISTRATION METHOD FOR JELMYTO

FDA-APPROVED METHOD OF ADMINISTRATION[1]

- Antegrade instillation via nephrostomy tube AND retrograde instillation via ureteral catheter can be used to administer JELMYTO in appropriate adult patients with low-grade UTUC

INVESTIGATED IN CLINICAL PRACTICE[3,4]

- Antegrade administration protocol evaluated in a real-world institution
- Safety and treatment response assessed in a multi-institutional review, analyzing diverse patient presentations

ADDRESSES THE NEEDS OF CERTAIN PATIENTS AND PRACTICES, SUCH AS[3,4]

- Patients who prefer an alternate method of instillation
- Those who cannot tolerate/prefer not to have anesthesia
- Practices that cannot accommodate weekly fluoroscopy or administration of anesthesia

Download the full Instruction Guide for instillation of JELMYTO with a nephrostomy tube

Download the order form for instillation of JELMYTO with a nephrostomy tube

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US-JEL-00772 06/23