Medical Information Request: JELMYTO® (mitomycin) for pyelocalyceal solution.
Thank you for your question regarding the OLYMPUS long-term follow-up study (BL007) and the 48-month duration of response.

Background:

The OLYMPUS LTFU (BL007) is a rollover study from the Phase 3 OLYMPUS trial (TC-UT-03, NCT02793128), which was the prospective, open-label, single-arm pivotal study of JELMYTO (mitomycin) for pyelocalyceal solution in 71 patients with treatment-naïve or recurrent non-invasive low-grade upper tract urothelial cancer (LG-UTUC). The purpose of the BL007 study is to evaluate long-term outcomes of primary chemoablation using UGN-101 in patients with LG-UTUC.

Study design:
Participants in the OLYMPUS trial (TC-UT-03, NCT02793128) who achieved a complete response (CR) after chemoablation with UGN-101 were followed quarterly for up to 12 months after initial CR. Patients with ongoing CR at study completion were asked to consent to collection of long-term follow-up data, for a maximum of 5 years, as they continued with standard of care disease management (Study BL007).

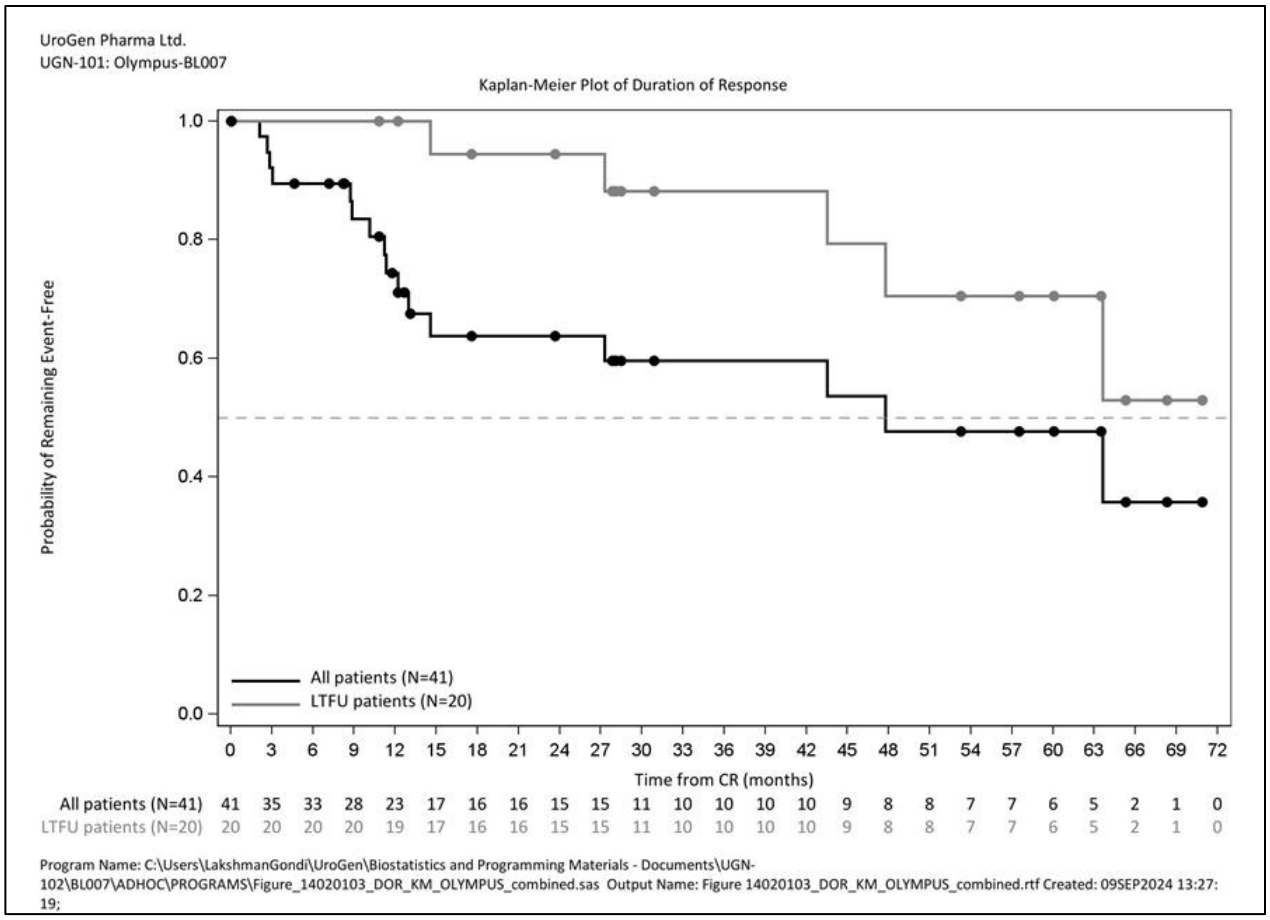
- There was no protocol-specified intervention or treatment in Study BL007 and no protocol-specified visits or evaluations. Supervising physicians provided semiannual updates on disease status for up to 5 years or until disease recurrence, progression, or death.
- Outcomes collected were duration of response (DOR), number of patients with recurrence of disease, number of patients with progression to high-grade disease, number of patients with UTUC who underwent nephroureterectomy, and number of deaths.
- The DOR was defined as the time from initial CR to recurrence, progression, or death. Patients were censored at the last adequate documented visit if an event had not been documented.
- Adverse events were not collected in the present rollover study. Adverse events were collected, and safety was established in the parent (OLYMPUS) trial.

Results:
Of the 71 patients enrolled in the parent (OLYMPUS) trial, 42 patients achieved complete response at the 3-month primary disease evaluation (4-6 weeks after completion of UGN-101 induction). One patient withdrew consent, and thus 41 patients with CR (58%; 95% CI, 45-69) entered the 12-month follow-up. At 12 months follow-up, 23 of the 41 patients remained in CR (56%; 95% CI, 40-72). Of these 23 patients with continued CR, 20 patients enrolled in the long-term follow-up trial (BL007). The most common adverse reactions (≥ 20%) reported in the OLYMPUS trial were ureteric obstruction, flank pain, urinary tract infection, hematuria, abdominal pain, fatigue, renal dysfunction, nausea, dysuria, and vomiting.

For the entire cohort of 41 patients achieving an initial CR in the OLYMPUS trial (58%; 95% CI, 45-69), including those followed in the long-term follow-up trial, the median duration of follow-up was 28.1 months (95% CI, 13.1-57.3), and the median DOR was 47.8 months (95% CI, 13.0-NE) as determined by Kaplan-Meier analysis. Documented events were reported in 16 of 41 patients (39%). Tumor recurrence occurred in 10 (24.4%) patients, of which 3 patients were treated with endoscopic ablation (data were not available for the remaining 7 patients). Six (14.6%) patients died; 1 death was related to UTUC; no deaths were related to study treatment. In this cohort, total of 25 (61%) participants were censored. One or more doses of UGN-101 maintenance therapy were administered to 29 (70.7%) patients.

Amongst the 20 patients enrolled in BL007, the median DOR was not estimable (NE; 95% CI, 43.5-NE) due to a low event rate based on a median duration of follow-up of 53.3 months (95% CI 27.9, 65.3). Two patients (10%) experienced tumor recurrence, and 3 (15%) died; no deaths were related to study treatment. A total of 15 patients (75%) were censored by the conclusion of the observation period. There were no reported progressions to high-grade disease. Two patients were reported as undergoing radical nephroureterectomy: one due to low-grade recurrent disease and one due to a nonfunctioning kidney.

400 Alexander Park Drive, 4th Floor, Princeton, NJ 08540 | 646-768-9780



Limitations:

Single-arm trial, inherent selection bias for the patients who achieved CR, and selection bias for the small number of patients that consented to be followed in the BL007 study.

Please refer to the attached 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, abdominal pain, fatigue, renal dysfunction, nausea, 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.

400 Alexander Park Drive, 4th Floor, Princeton, NJ 08540 | 646-768-9780

References:

1. JELMYTO® (mitomycin) for pyelocalyceal solution. Prescribing Information 2024. UroGen Pharma, Princeton, New Jersey.
2. Kleinmann N, 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. Matin S, 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.
4. Data on file. UroGen Pharma.

Attachments:

- JELMYTO® (mitomycin) for pyelocalyceal solution. Prescribing Information 2024

400 Alexander Park Drive, 4th Floor, Princeton, NJ 08540 | 646-768-9780