Poster Session 4: Oncology–Bladder, Renal, Testes
Friday, October 10, 2025 • 7:00–8:00 am

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Abstract #46

Preliminary results from LEGEND: A phase 2 study of detalimogene voraplasmid, a novel, investigational, non-viral genetic medicine for high-risk non-muscle invasive bladder cancer (NMIBC)

Badar Mian[1], Girish S. Kulkarni[2], Wassim Kassouf[3], Ricardo A. Rendon[4], Vignesh T. Packiam[5], Sam S. Chang[6], Shreyas Joshi[7], Jen-Jane Liu[8], Anne Schuckman[9], Ashish Kamat[10], Raj Satkunasivam[11], Neal Shore[12], Rian Dickstein[13], Amir Salmasi[14], Vikram Narayan[7], John A. Taylor[15], Yair Lotan[16], Alberto Martini[17], Christine Tosone[18], Anthony Cheung[19], Katherine Chan[18], Raj Pruthi[18], Mark Tyson[20]

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Introduction: Detalimogene voraplasmid (EG-70) is a novel, investigational, non-viral genetic medicine for high-risk NMIBC, including BCG-unresponsive disease. The phase 1 portion of LEGEND (NCT04752722) demonstrated a promising safety profile and an overall complete response (CR) of 73% at any time. Phase 2 is ongoing; preliminary efficacy results of the pivotal cohort 1 (BCG-unresponsive NMIBC with CIS) and safety for all cohorts are reported here.

Methods: Key eligibility criteria: ≥18 years; ECOG PS 0−2; high-risk NMIBC, ± resected coexisting papillary (Ta/T1) tumors, ineligible for/elected not to undergo cystectomy. Cohorts: BCG-unresponsive with CIS (pivotal cohort 1); BCG-naive with CIS (cohort 2A); BCG-exposed with CIS (cohort 2B); BCG-unresponsive with high-grade papillary disease without CIS (cohort 3). Patients received four doses, 50 mL intravesically at weeks 1, 2, 5, and 6 of a 12-week cycle x four cycles. Primary endpoint: CR rate at weeek 48; safety. Secondary endpoints: PFS; CR rate at week 12, 24, 36, and 96, % of patients with a durable CR at 12 months.

Results: As of September 13, 2024, 21 patients were evaluable for efficacy in cohort 1. In the 42 safety-evaluable patients (all cohorts), treatment-related adverse events were observed in 20 (47.6%; all G1/2), most commonly (≥10%): dysuria (21.4%); bladder spasm (19.0%); pollakiuria (11.9%); and fatigue (11.9%). Overall CR rate 71%; CR rate 67% at three months and 47% at six months.

Conclusions: Preliminary data from the pivotal phase 2 portion of LEGEND suggest a promising safety/tolerability profile. Overall, 71% of patients achieved a CR, with 67% achieving a CR at three months and 47% achieving a CR at six months.

Funding: enGene Inc.

Abstract #47

Mechanism of action and translation to the clinic of detalimogene voraplasmid: A novel, investigational, non-viral genetic medicine for non-muscle-invasive bladder cancer (NMIBC)

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Introduction: Detalimogene voraplasmid (EG-70) is a novel, investigational, non-integrating, non-viral genetic medicine designed to elicit local stimulation of an anti-tumor, intravesical immune response while mitigating risk of systemic toxicities. LEGEND is an ongoing phase 1/2 study (NCT04752722) investigating safety and efficacy of detalimogene in high-risk NMIBC.

Methods: Preclinical evaluation was conducted in vitro and in vivo in an orthotopic syngeneic model of bladder cancer. Immunocompetent C57BL/6 mice received two weekly intravesical instillations of a murine EG-70 surrogate (mEG-70). Efficacy was assessed by flow cytometry, immunoassays, immunohistochemistry, bioluminescence in vivo imaging, and overall survival. The phase 1 clinical LEGEND study evaluated detalimogene in high-risk BCG-unresponsive NMIBC with carcinoma in situ (CIS).

Results: Immune profiling revealed remodeling of the tumor microenvironment from an immunosuppressive to a pro-inflammatory milieu. Accordingly, administration of mEG-70 was associated with a marked and dose-dependent reduction in tumor burden. Over 90% of mEG-70-treated mice had durable anti-tumor responses, as demonstrated by long-term disease-free survival, with no disease relapse during the 100-day monitoring period. The anti-tumor immune response in surviving tumor-free mice resulted in durable protection against subsequent tumor re-challenge, and systemic immune memory. In phase 1 of LEGEND, detalimogene was generally well-tolerated, with a complete response rate of 73% at any time in patients with BCG- unresponsive NMIBC with CIS.

Conclusions: In a preclinical model, a mouse surrogate of detalimogene elicited a durable, anti- tumor immune response and a marked, dose-dependent reduction in tumor burden. The proposed mechanism of action of detalimogene has been translated clinically into the phase 1 portion of the LEGEND study.

Funding: enGene Inc.

Abstract #48

Effective criteria for identifying higher-risk small renal masses that require treatment during active surveillance

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Introduction: The oncologic safety of active surveillance (AS) for small renal mass (SRM) patients has become increasingly clear; however, uniform agreement is still lacking as to which tumor features indicate progression and should be used to trigger delayed intervention (DI). Ideal progression criteria for intervention (PCI) would selectively treat SRM with adverse pathology (15–25% of all SRM), given a higher risk for metastatic potential. We previously described our AS experience using predefined PCI to prospectively trigger DI. The current study aimed to update our pathologic outcomes of DI nephrectomy cases in order to determine the efficacy of our PCI thresholds for identifying SRMs with adverse pathology for treatment.

Methods: From January 2013 to April 2024, all PCI-free SRM patients presenting to a single urologist at a comprehensive cancer center were recommended AS using a predefined PCI panel. DI was recommended during AS only upon new PCI development. PCI were defined prospectively as any SRM-related symptoms, unfavorable biopsy histology, cT3a stage, or any of the following without benign neoplastic biopsy histology: longest tumor diameter (LTD) >4 cm; growth rate (GR) >5 mm/year for LTD up to 3 cm; and GR >3 mm/year for LTD over 3 cm. Rates of adverse pathology were retrospectively assessed for all AS patients undergoing DI by either partial or radical nephrectomy.

Results: Of 388 SRM patients with 50 months median followup on AS, 67 (17%) underwent DI, including 62 (92%) by partial (53, 79%) or radical (9, 13%) nephrectomy and five (7%) by cryoablation. All (62/62 100%) DI resection cases showed malignant pathology, with histologic subtypes including clear-cell (52, 84%), papillary (7, 11%), chromophobe (2, 3%), and unclassified (1, 1.6%). Most (33/62, 53%) DI resections contained adverse pathology, including 28 (45%) with grade ≥3 and 11 (17%) with pT3a.

Conclusions: Prospectively applied PCI defined herein appear to effectively identify high-risk SRM cases for DI conversion, given notably higher rates of adverse pathology in DI resections relative to rates historically reported for SRM resections. PCI described herein should be studied further as a potential standard for determining progression during AS.

Abstract #49

Applying user-centered design to optimize delivery of a post-cystectomy remote monitoring program

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Introduction: The post-cystectomy period is defined by distinct characteristics and challenges that render patients uniquely vulnerable. While remote monitoring interventions show promise in improving clinical outcomes in some contexts, such programs following cystectomy have not effectively reduced readmissions. This may be because these programs are not tailored to the unique needs of cystectomy patients. To overcome these barriers, we applied user-centered design methods to incorporate patient feedback into a more useful remote monitoring intervention prototype.

Methods: We recruited members of a bladder cancer survivorship group who had undergone cystectomy to participate in user-centered design sessions to refine a post-cystectomy remote monitoring prototype. Participants were provided access to the prototype smartphone application and paired wearable device. We reviewed key features of the program via think aloud and cognitive walkthrough protocols. Participant feedback was organized by theme and frequency by two reviewers using a hybrid deductive-inductive approach.

Results: We included 20 participants, 25% male, with a mean age of 68.8 years old. Participants underwent cystectomy on average three years prior. Preliminary analysis revealed three primary themes across participant feedback. First, people were interested in receiving action-oriented guidance from the remote monitoring program, especially when postoperative issues were identified: "Getting the treatment, that's what's important. I need to know what to do. Especially in those first 30 days. In those first 30 days your mind is just…it's so stressful. It's so tressful" (patient 1). Next, they discussed using the program for specific and provider-verified recommendations. Finally, they valued visual progress indicators with educational resources to help them monitor their recovery independently.

Conclusions: Integrating user-centered design into remote monitoring intervention development is critical to creating a functional and supportive program that engages and empowers patients following cystectomy. The initial feedback from this study will inform ongoing iterative improvements in the intervention prototype, ensuring it aligns with patient needs and is optimizing for long-term care.

Funding: 2024 Urology Care Foundation Research Scholar Award Program and the American Urological Association Northeastern Section for KM, and NIH DK111011 for KDS.

Abstract #50

Under-reporting of carcinoma in situ in patients with high-grade papillary non-muscle- invasive bladder cancer (NMIBC)

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Introduction: Patients with high-grade Ta/T1 NMIBC often have concomitant carcinoma in situ (CIS); however, the rate is variable, and pathologists may not examine every bladder biopsy once a high-grade papillary lesion is identified. Newer drugs for patients with bacillus Calmette-Guérin-unresponsive NMIBC, such as nadofaragene firadenovec-vncg (ADSTILADRIN®), have a label indication for those with CIS ± papillary tumors. Therefore, failure to report CIS may impact access to therapy. We studied the incidence of CIS in a cohort of patients with high-grade Ta/T1 NMIBC in a private practice setting.

Methods: Pathology specimens from transurethral resections in 2024 from patients at Arkansas Urology with a diagnosis of high-grade papillary NMIBC without CIS were reviewed by one pathologist (AC), with review of all bladder biopsies and incidence of CIS reported.

Results: There were 328 patient samples reviewed. Mean patient age was 73 years (range 47–93), and 80.5% were male. Presurgical diagnosis ICD-10 codes indicated bladder malignancy (C67.x) or hematuria (R31.0), but only two cases referenced CIS (D090). Overall, 84 cases (26%) showed CIS on re-review. Among the five pathologists who initially reviewed the cases, CIS-positive rates varied from 0% (0/9) to 67% (20/30).

Conclusions: Based on this single-center study, approximately one-quarter of high-grade Ta/T1 specimens may have initially unreported CIS. Good communication between urologist and pathologist is essential to request a specific ruling out of CIS in all bladder fragments, as a diagnosis of CIS in addition to high-grade papillary disease may impact therapeutic options for the patient according to FDA labels and NCCN guidelines.

Funding: Ferring Pharmaceuticals, Inc.

Abstract #51

Comparing AI-dependent and AI-assisted approaches to extract information about renal masses from radiology reports

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Introduction: The natural history of suspicious renal masses remains poorly characterized. Valuable data can be found in radiology reports, but non-manual data extraction is challenging due to format inconsistencies. Artificial intelligence (AI)-based approaches show promise to overcome these limitations. The objective of this study was to better understand best use for AI-based approaches for renal mass data extraction from radiology reports.

Methods: We identified CT, MRI, and ultrasound reports potentially related to suspicious renal masses from a multihospital academic network. Two extraction strategies were compared: 1) AI-dependent, where a pretrained large language model (LLM) (ChatGPT-4o) was applied to the full text of the report for mass identification and extraction of characteristics (cystic vs. solid, multiplicity, and size); and 2) AI-assisted, where reports were first segmented, followed by staged LLM application to initially identify reports with masses and then extract characteristics. We evaluated the impact of in-context examples (0, 10, 20, 30, 40, and 50 examples). Performance was benchmarked against manual review of 600 randomly selected reports and assessed using F1 score and accuracy.

Results: Across all tasks, performance improved with examples in the range of 30–40 examples and then began to plateau or decrease. For detecting suspicious renal masses, the AI-assisted strategy achieved an F1 score of 0.934 and accuracy of 0.970 with 40-shot examples, outperforming the AI-dependent approach (F1 0.910, accuracy 0.960). In classifying cystic masses, both approaches performed well, with the AI-assisted method reaching an F1 score of 0.750 and accuracy of 0.960 with 30-shot examples. Multiplicity detection favored the AI-assisted approach with 40-shot examples (F1 0.677, accuracy 0.973), compared to the AI- dependent (F1 0.667, accuracy 0.972). Tumor size extraction showed high performance across strategies, with F1 scores exceeding 0.882 and accuracy over 0.948. The AI-assisted approach demonstrated greater stability across all tasks.
Conclusions: AI-based approaches demonstrated strong performance for extracting information from radiology reports about suspicious renal masses. Performance gradually improved with increasing in-context examples but then plateaued or decreased with further examples. Furthermore, an AI-assisted, staged–extraction approach generally outperformed a single-step, AI–dependent approach. Our findings demonstrate how AI-based approaches can be optimized to extract information from free-text clinical reports. These approaches show promise for large-scale applications in characterizing the natural history of renal masses.
Funding: All publications and presentations involving use of CTSI resources must cite the following grant number: NIH/NCATS UL1TR001445.

Abstract #52

Poor glycemic control is associated with pathological upstaging in renal cell carcinoma

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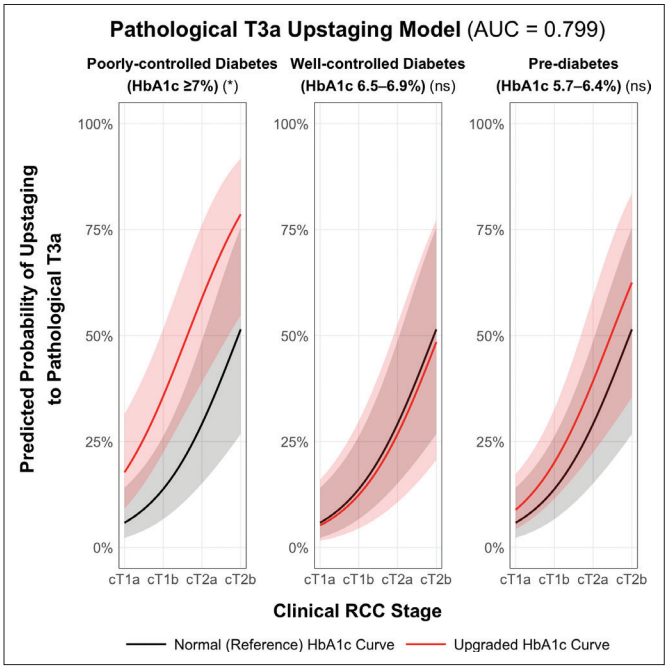
Introduction: Localized clinical stage T1–T2 (cT1–T2) renal cell carcinoma (RCC) is upstaged to pathological T3a in up to 19% of cases, which is associated with a worse prognosis. Diabetes is a suggested risk factor for pathological upstaging, yet the impact of glycemic control remains uncertain. We aimed to assess the association between hemoglobin A1c (HbA1c) and pathological upstaging to T3a in patients with cT1–T2 RCC.
Methods: We conducted a single-center, retrospective cohort study of adult patients treated with partial or radical nephrectomy from 2019–2022. We included patients with HbA1c within 90 days of preoperative imaging. Clinical and pathological stages were assigned using imaging and pathology reports, respectively. Non-RCC and non-cT1–T2 RCC tumors were excluded. For patients with multiple HbA1c, the values were averaged. Patients were categorized as normal (HbA1c <5.7%), pre-diabetes (5.7–6.4%), well-controlled diabetes (6.5–6.9%), or poorly controlled diabetes (≥7%). We fit a logistic regression model to predict clinical T1–T2 to pathological T3a upstaging, adjusted for HbA1c category, preoperative clinical stage, days between imaging and surgery, body mass index (BMI), age, and gender. Model performance was evaluated using the area under the curve (AUC).
Results: We identified 268 patients with cT1–T2 RCC. Of these, 168 (63%) were male. The mean age was 64.5 years, and the mean BMI was 32.7. Most patients had normal or prediabetic range HbA1c, with 75 (28%) and 92 (34%) in these respective categories, while 39 (15%) had well-controlled diabetic range and 62 (23%) had poorly controlled diabetic range HbA1c. Based on preoperative imaging, 229 (85%) patients were clinical stage T1. Post-resection pathological upstaging to T3a occurred in 46 (17%) patients. The model showed good discrimination (AUC 0.799). Significant predictors of upstaging were poorly-controlled diabetes (odds ratio [OR] 3.47, 95% confidence interval [CI] 1.30–9.57) (Figure 1), preoperative clinical stage (OR 2.58,
95% CI 1.59–4.33), and, marginally, age at imaging (OR 1.04, 95% CI 1.01–1.09).
Conclusions: Poorly controlled diabetic range HbA1c is associated with increased odds of pathological upstaging from clinical T1–T2 to pathological T3a. Therefore, clinicians may consider adopting a lower threshold for transitioning from active surveillance to intervention for patients with poor glycemic control and suspected localized RCC.
Funding: Murali Kovvur was partially supported by the NIH T35 (DK065521) and the Henry L. Hillman Foundation Fellows for Innovative Cancer Research programs.



Abstract #52. Figure 1. Pathological T3a upstaging model (AUC=0.799).

Abstract #53

Automated extraction of pathologic stage for renal cell carcinoma from the electronic medical record using a deep phenotype natural language processing model

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Introduction: The electronic medical record (EMR) is being increasingly used in health services research for large-scale datasets, compared to historic use of claims data; however, manual extraction of cancer phenotypes from the EMR, including tumor, nodes, and metastases (TNM) staging, is laborious and limited to use in small datasets. We sought to determine the feasibility of using a deep-phenotype (DeepPhe) natural language-processing model to assign pathologic TNM stage using EMR data for renal cell carcinoma (RCC).
Methods: We identified a cohort of patients at a single institution between 2019–2023 who underwent partial or radical nephrectomy for renal mass. Patients with non-RCC histology or multiple tumors were excluded. Pathologic TNM stage was obtained via expert manual review of EMR pathology reports. The DeepPhe natural language-processing model was then applied to the same cohort, using clinical documents and discrete EMR data to assign a pathologic TNM stage for RCC. Cohen's Kappa was then used to determine accuracy and interrater reliability of DeepPhe in assigning pathologic stage, compared to expert manual review. Kappa statistics were interpreted as follows: below 0.2 indicates poor agreement, 0.2–0.4 fair, 0.41–0.6 moderate, 0.61–0.8 substantial, and above 0.8 excellent agreement. Additionally, given the ordinal nature of pathologic stage, we applied weights to reflect the importance of close agreement, which provides partial credit for near agreement.
Results: A total of 79 patients were included in the analysis, with a distribution of pathologic T stages: pT1 (n=34, 43%), pT2 (n=10, 13%), pT3 (n=32, 41%), and pT4 (n=3, 4%). The overall Kappa for the entire cohort was high, with an unweighted Kappa of 0.94 (95% confidence interval [CI] 0.87, 0.99) and a weighted Kappa of 0.99 (95% CI 0.99, 1.00), indicating excellent agreement between DeepPhe and expert manual review. When stratified by pathologic T stage, concordance

rates were 100% for each category. Additionally, detailed concordance rates across specific pathologic substages (e.g., pT1a, pT3a) showed near-perfect agreement for most stages, with some variation within nodal staging (e.g., pT3aN1) showing 66.7% concordance.
Conclusions: The DeepPhe natural language-processing model demonstrates high accuracy and reliability in determining pathologic stage for RCC using EMR data. Implementing this model in large-scale projects with EMR data use may substantially reduce or eliminate need for manual review. The DeepPhe system can be found at https://deepphe.github.io.
Funding: NCI Grant U24CA248010.

Abstract #54

LEGEND: A phase 1/2 study of detalimogene voraplasmid intravesical monotherapy for patients with high-risk non-muscle-invasive bladder cancer (NMIBC)

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Introduction: Detalimogene voraplasmid (EG-70) is a novel, investigational genetic medicine for high-risk non-muscle-invasive bladder cancer (NMIBC) delivered intravesically using a non-viral vector. It is designed to elicit local stimulation of anti-tumor immune responses in the bladder without cellular integration, mitigating the risk of systemic toxicity. The phase 1 (dose-escalation) portion of the first-in-human, phase 1/2, open-label, multicenter study of detalimogene (LEGEND; NCT04752722) is complete. The phase 2 dose was identified, treatment was generally well-tolerated, and the overall complete response (CR) rate was 73%. Here we describe the ongoing phase 2 portion of the study, which opened in May 2023.
Methods: Eligibility criteria: age ≥18 years; ECOG PS 0−2; NMIBC ± resected coexisting papillary (Ta/T1) tumors, ineligible for/elected not to undergo, cystectomy; satisfactory bladder function with ability to retain study drug for ≥60 minutes. Cohorts: BCG-unresponsive with CIS (pivotal cohort 1); BCG-naive with CIS (cohort 2A) or BCG-exposed with CIS (cohort 2B); BCG-unresponsive with high-grade papillary disease without CIS (cohort 3). Patients receive detalimogene (dose: 0.8 mg/mL) in a volume of 50 mL intravesically at weeks 1, 2, 5, and 6 in a 12-week cycle x four cycles; patients with CR at end of fourth cycle enter maintenance treatment (two instillations per cycle, at weeks 1 and 2 for up to eight cycles). Phase 2 primary endpoints: efficacy (CR rate at week 48); safety. Secondary endpoints: PFS; CR rate at weeks 12, 24, 36, and 96; % of patients with durable CR at 12 months. The phase 2 portion of the study is enrolling and will recruit approximately 300 patients across all cohorts, from sites in the U.S., Canada, Europe, and the Asia-Pacific region.
Results/Conclusions: To come
Funding: enGene Inc.

Abstract #55

The HistoSonics Edison™ system for the treatment of primary solid renal tumors using histotripsy: #HOPE4KIDNEY US

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Introduction: Histotripsy is a novel treatment option that may have advantages over existing kidney-directed therapies, including truly non-invasive therapy without percutaneous devices, as well as precise and predictable treatment zones guided by real-time imaging. Histotripsy results in homogeneous destruction of the prescribed planned treatment volume (PTV) and preserves critical structures within or adjacent to the treatment volume. The FDA cleared histotripsy for the non-invasive destruction of liver tumors based on the safety and efficacy results of the #HOPE4LIVER clinical trial in October 2023. The #HOPE4KIDNEY US trial will evaluate the effectiveness and safety of histotripsy using the HistoSonics Edison System for the destruction of kidney tissue by treating primary solid renal tumors ≤3 cm (ClinicalTrials.gov: NCT05820087).
Methods: #HOPE4KIDNEY US is a prospective, multicenter, single-arm pivotal trial designed to evaluate the effectiveness and safety of the HistoSonics Edison System for the destruction of kidney tissue by treating primary solid renal tumors. The primary effectiveness endpoint is primary technique efficacy at 90 days, defined as the percentage of targeted tumors that were successfully eliminated after a single histotripsy session as assessed by contrast enhanced MRI or CT and will be centrally confirmed. Renal tumors must be ≤3 cm in maximum diameter, with biopsy confirming pathology type. The primary safety endpoint is freedom from index procedure related major complications, defined by Clavien-Dindo classification grade 3 or higher up to 30 days after the histotripsy procedure. The trial is powered to evaluate the co-primary endpoints of effectiveness and safety against performance goals of 75% established from renal ablation literature; results must be positive for both co-primary endpoints for the trial to be considered successful. Total enrollment will be up to 68 subjects, targeting 54 evaluable subjects. Subjects will have followup visits at 14, 30, 90, and 180 days, and annually thereafter up to five years post-procedure. #HOPE4KIDNEY US is sponsored and financed by HistoSonics. Key trial eligibility criteria require subjects to be ≥22 years of age and diagnosed with only one non-metastatic solid renal mass ≤3 cm confirmed via CT or MRI. The subject must have an adequate acoustic window to visualize the targeted tumor using the HistoSonics Edison System and the targeted tumor with adequate margin (PTV) cannot overlap the renal pelvis, main renal vessel, ureter, or other vital structures.
Results: Fifty-five subjects have been enrolled at 10 sites as of April 16, 2025.
Conclusions: To come.

Abstract #56

Long-term outcomes of treatment of low-grade upper tract urothelial carcinoma with UGN- 101, a mitomycin reverse thermal gel

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Introduction: Endoscopically guided ablation is commonly used to treat low-grade upper tract urothelial carcinoma (LG-UTUC). Long-term endoscopic surveillance is needed due to the recurrent nature of UTUC. We report data from a noninterventional five-year long-term followup (LTFU) study of patients who achieved complete response (CR) following treatment with UGN-101, a reverse thermal gel containing 4 mg mitomycin per mL, in the phase 3 OLYMPUS trial (NCT02793128).
Methods: Patients who participated in OLYMPUS and achieved a CR after six once-weekly doses of UGN-101 were followed for up to 12 months after initial CR. Those still in response at 12 months could enroll in the LTFU study. Outcomes

included Kaplan-Meier estimate of duration of response (DoR) and disease recurrence/progression. Supervising physicians provided semiannual updates on patients' disease status.
Results: A total of 71 patients enrolled in OLYMPUS (68% male, 87% White, median age 71 years), and 42 achieved CR ~3 months after study initiation. Among 41 patients followed after initial CR (one withdrew consent), including 20 who entered the five-year LTFU, median followup was 28.1 months (95% CI 13.1–60.1) and median estimate of DoR was 47.8 months (95% CI 13.0–not estimable [NE]). Among the 20 patients with LTFU, median followup was 53.3 months (95% CI 27.9–72.8) and median DoR was NE (95% CI 43.5–NE) due to a low event rate. During LTFU, two (10%) patients experienced LG-UTUC tumor recurrence; three (15%) died (unrelated to study treatment); and seven (35%) discontinued. Five (25%) patients were in ongoing CR at the end of the five-year LTFU study with the longest reported DoR of 82.6 months.
Conclusions: Patients with LG-UTUC who achieved CR after receiving treatment with UGN-101 experienced clinically meaningful long-term response, with a median estimate of DoR of 47.8 months. The ongoing uTRACT registry (NCT05874921) is collecting real-world data in a larger patient population (n=400) to further inform the use of UGN-101 in UTUC patients.
Funding: UroGen Pharma. Pharmaceutical/Biotech Company.

Abstract #57

PENELOPE: Tissue penetration of gemcitabine phosphate metabolites following TAR-200 administration vs. standard intravesical instillation in minipigs

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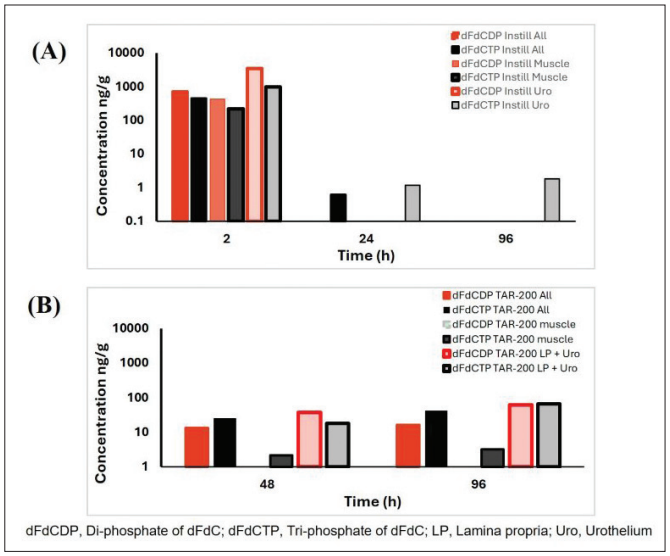
Introduction: TAR-200 is a novel intravesical (IVes) targeted releasing system designed to provide local continuous/sustained release of gemcitabine within the bladder, with potentially deep-tissue penetration. This preclinical study evaluated the penetration of gemcitabine (dFdC) and its active metabolites, diphosphate and triphosphate of dFdC (dFdCDP, dFdCTP), in bladder tissues up to 96 hours (h) after TAR-200 administration or intravesical instillation.
Methods: Bladder tissue concentrations of gemcitabine and its active metabolites were measured in five minipigs following gemcitabine administration either by intravesical or TAR-200 instillation. Three animals received a two-hour bolus intravesical instillation of 2 g free base-equivalent (FBE) of gemcitabine hydrochloride dissolved in saline (40 mg/mL), with tissue collection from one animal at two hours, a second animal at 24 hours, and a third animal at 96 hours. The TAR-200 delivery system, containing 225 mg FBE, was placed into the bladder of two animals, where it remained until tissue collection at 48 hours and 96 hours, respectively. At necropsy, samples of dome, left and right lateral wall, and trigone were collected and the urothelium with underlying lamina propria were separated from the muscle layer of the urinary bladder. Results were reported as the mean of the four tissue samples collected.
Results: Following intravesical delivery of gemcitabine (two hours), total bladder tissue concentrations of the active phosphorylated metabolites of gemcitabine were high and were detected in all bladder layers but were virtually undetectable in samples after 24 hours and 96 hours (Figure 1A). When delivered with the TAR-200 system, gemcitabine active metabolites could be detected in all bladder layers over the investigated indwelling period up to 96 hours (Figure 1B).
Conclusions: Following administration of gemcitabine using the TAR-200 delivery system, measurable levels of active phosphorylated metabolites were detected in all bladder layers, including the urothelium/lamina propria and muscle at 48 hours and 96 hours. Comparatively, tissue exposure to gemcitabine delivered through a bolus instillation over a two-hour indwelling period is limited by its short half-life (<3 hours), with little evidence of gemcitabine active metabolites in bladder tissue by 24 hours. Results of this study demonstrate that sustained local delivery of gemcitabine to the bladder through the TAR-200 system can deliver active metabolites to all layers of the bladder at least four days following TAR-200 placement.
Funding: Janssen Research and Development, LLC, a Johnson and Johnson company.



dFdCDP, Di-phosphate of dFdC; dFdCTP, Tri-phosphate of dFdC; LP, Lamina propria; Uro, Urothelium

Abstract #57. Figure 1. Mean dFdCDP and dFdCTP concentrations in bladder tissue layers following gemcitabine delivery by (A) intravesical instillation and (B) TAR-200.

Abstract #58

Impact of tumor burden or focality in recurrent low-grade intermediate-risk non-muscle invasive bladder cancer on durability of complete response to treatment with UGN-102

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Introduction: In the single-arm ENVISION pivotal phase 3 study (NCT05243550) patients with low-grade intermediate-risk non-muscle-invasive bladder cancer (LG-IR-NMIBC) were treated with UGN-102, a reverse thermal hydrogel containing mitomycin. Complete response rate (CRR) at three months was 79.6%, with an 80.6% probability of remaining in response 18 months later by Kaplan-Meier estimate. Here, we present an analysis evaluating if tumor focality or tumor burden influenced response rate and/or durability.
Methods: A total of 240 patients with recurrent LG-IR-NMIBC received at least one dose of UGN-102; 95% (228) received all six doses. Three months after the first dose, patients were examined for the presence of bladder cancer using cystoscopy, urine cytology, and for-cause biopsy. Patients achieving complete response (CR) underwent followup with surveillance cystoscopy/cytology. In prespecified subgroups, comparisons of patients with tumor burden (calculated as the sum of the diameters of all visible tumors) ≤3 cm vs. >3 cm and solitary vs. multifocal tumors were performed for CRR at three months and hazard ratios (HRs) of duration of response (DoR) at 18 months after achieving CR. For the comparison of CRR, p-values were calculated using Fisher's exact test. HRs of DoR were calculated using a Cox proportional hazards model, and p-values calculated using a log-rank test. Subgroup comparisons were not powered to identify a difference and p-values were unadjusted for multiple comparisons.
Results: CRR at three months was 82.7% vs. 73.8% for patients with tumor burden ≤3 cm and >3 cm, respectively. Of patients with CR at three months with tumor burden ≤3 cm and >3 cm, 18.2% vs. 25.8%, respectively, experienced either recurrence of LG disease, progression (either stage or grade), or death 18 months after CR. In patients with multifocal vs. solitary tumors, three-month CR was 79.4% vs. 82.5%; recurrence rates were 21.5% vs. 15.2%. DoR HRs were not statistically significant for any comparison made.

Conclusions: The CRR and DoR were robust in all subgroups and no significant differences were observed based on tumor burden or focality. Study limitations were the small sample size of comparator groups, and single-arm study design. UGN-102 is potentially a valuable non-surgical treatment option for many patients with LG-IR-NMIBC.
Funding: UroGen Pharma.

Abstract #58. Table 1

	CR at 3 months	CR ratio (95% CI) p	Recurrence within 18 months after CR	DoR HR (95% CI) p
Tumor burden				0.715 (0.325, 1.575) p=0.4034[a]
≤3 cm	82.7% (148/179)	1.12 (0.92, 1.36) p=0.1945[a]	18.2% (27/148)	
>3 cm	73.8% (31/42)		25.8% (8/31)	
Tumor count				1.442 (0.564, 3.687) p=0.4412[a]
Multifocal	79.4% (158/199)	0.96 (0.82, 1.13) p=0.8292[a]	21.5% (34/158)	
Solitary	82.5% (33/40)		15.2% (5/33)	

[a]3-month CR patients only. bNominal, Fisher's exact test for CRR ratio, and log-rank test for DoR HR.

Abstract #59

Outcomes of robot-assisted radical cystectomy for de novo muscle invasive bladder cancer versus progression of non-muscle invasive bladder cancer

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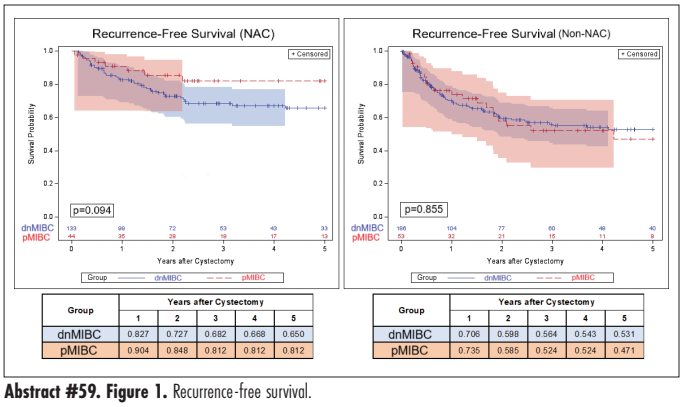
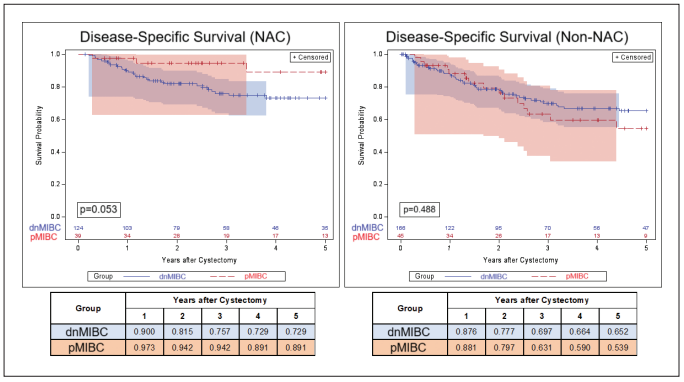
Introduction: We aimed to investigate the oncologic outcomes of robot-assisted radical cystectomy (RARC) for de novo muscle-invasive bladder cancer (dnMIBC) vs. MIBC after progression of non-muscle-invasive bladder cancer (pMIBC).
Methods: We conducted a retrospective review of our quality assurance RARC database between 2005 and 2024. Patients with ≥cT2 were identified and divided into dnMIBC (≥cT2 on their first transurethral resection [TURBT]) vs. those with pMIBC (progressed to ≥cT2 from NMIBC). Kaplan-Meier method was used to depict recurrence free (RFS), disease specific (DSS), and overall survival (OS).
Results: A total of 416 patients underwent RARC (77% had dnMIBC and 23% pMIBC). Patients with dnMIBC had ≥pT3 more frequently (53% vs. 40%, p=0.037), but with similar variant histology involvement (53% vs. 42%, p=0.083), pN+ (31% vs. 25%, p=0.255) and positive margins (9% vs. 11%, p=0.563). pMIBC group exhibited similar RFS, DSS, and OS if they received cystectomy directly (p=0.855 for RFS, p=0.488 for DSS, and p=0.840 for OS); however, the pMIBC group tend to benefit more from neoadjuvant chemotherapy (NAC) if administrated. With NAC, pMIBC group showed better five-years RFS and DSS but didn't reach statistical significance (RFS: 81% vs. 65%, log rank p=0.094; DSS: 89% vs. 73%, log-rank p=0.053) (Figures 1, 2, 3).
Conclusions: Patients who progressed to MIBC from NMIBC seem to have a better response to NAC than patients with de novo MIBC.
Funding: Roswell Park Alliance Foundation.



Group	Years after Cystectomy 1	2	3	4	5
dnMIBC	0.827	0.727	0.682	0.668	0.650
pMIBC	0.904	0.848	0.812	0.812	0.812

Group	Years after Cystectomy 1	2	3	4	5
dnMIBC	0.706	0.598	0.564	0.543	0.531
pMIBC	0.735	0.585	0.524	0.524	0.471

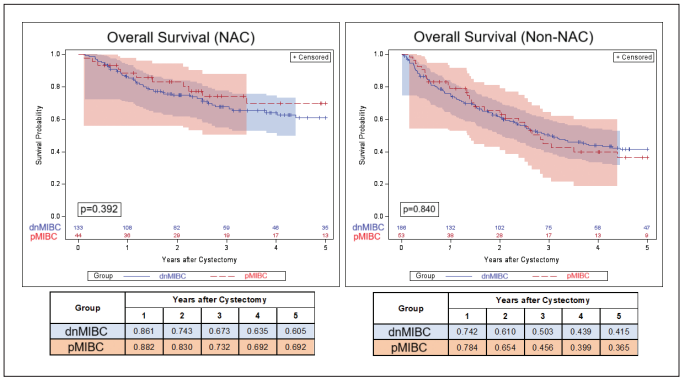
Abstract #59. Figure 1. Recurrence-free survival.



Group	Years after Cystectomy 1	2	3	4	5
dnMIBC	0.900	0.815	0.757	0.729	0.729
pMIBC	0.973	0.942	0.942	0.891	0.891

Group	Years after Cystectomy 1	2	3	4	5
dnMIBC	0.876	0.777	0.697	0.664	0.652
pMIBC	0.881	0.797	0.631	0.590	0.539

Abstract #59. Figure 2. Disease-specific survival.



Group	Years after Cystectomy 1	2	3	4	5
dnMIBC	0.861	0.743	0.673	0.635	0.605
pMIBC	0.882	0.830	0.732	0.692	0.692

Group	Years after Cystectomy 1	2	3	4	5
dnMIBC	0.742	0.610	0.503	0.439	0.415
pMIBC	0.784	0.654	0.456	0.399	0.365

Abstract #59. Figure 3. Overall survival.

Abstract #60

Does second-look TURBT for high-risk non-muscle-invasive bladder cancer improve response to adjuvant intravesical therapy?

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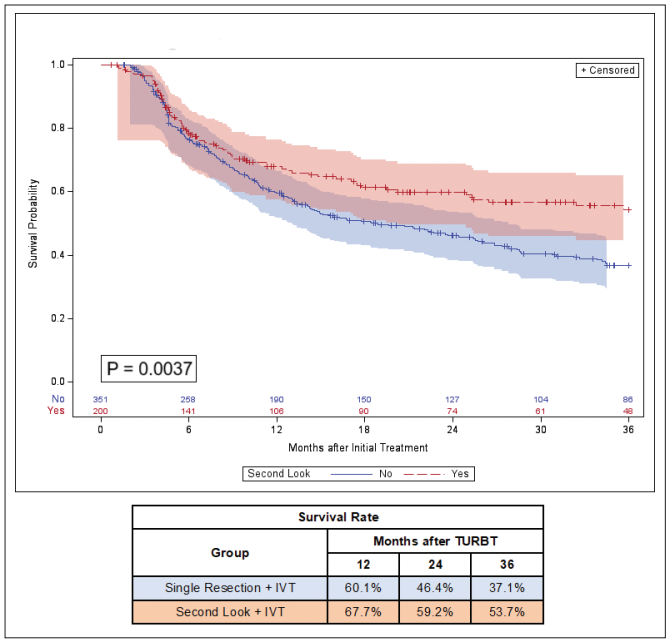
Introduction: We aimed to investigate whether second-look transurethral resection (re-TURBT) of Bladder Tumor (TURBT) for high-risk non-muscle-invasive bladder cancer (NMIBC) improves response to adjuvant intravesical therapy (IVT).

Methods: We conducted a retrospective review of our quality assurance TURBT database between 2000 and 2024. All patients with high-risk NMIBC who received IVT were included in the study. Re-TURBT was defined as TURBT within eight weeks of the initial TURBT. Patients were divided into those who received re-TURBT vs. those who did not. Patients were followed as per AUA/SUO/EAU guidelines with cystoscopy and urine cytology every three months for the first two years, then every six months for years 3–5, then annually thereafter. Annual upper tract imaging was also performed. Kaplan-Meier method was used to depict high-grade recurrence free survival (RFS).

Results: A total of 551 patients were included in the study; 36% received re-TURBT. The median time between initial and re-TURBT was 6.0 weeks (IQR 4.1–7.4 weeks). Indications for re-TURBT included incomplete resection (10%), absence of detrusor in specimen (36.5%), T1 high-grade disease (32.5%), CIS disease (5.5%), and Ta high-grade (15.5%). Re-TURBT patients who received IVT exhibited improved HGRFS of 68% and 54% at one and three years, respectively, compared to 60% and 37% for those who did not receive re-TURBT (log rank $p<0.01$) (Figure 1).

Conclusions: Patients with high-risk NMIBC who received a re-TURBT prior to IVT exhibited improved HGRFS compared to those who received IVT without re-TURBT; 62% of re-TURBT were found to have residual disease, of whom 17% upstaged.

Funding: Roswell Park Alliance Foundation.



Survival Rate			
Group	Months after TURBT		
	12	24	36
Single Resection + IVT	60.1%	46.4%	37.1%
Second Look + IVT	67.7%	59.2%	53.7%

Abstract #60. Figure 1. High-grade recurrence-free survival.