Duravelo-2 Clinical Trial

(BT8009-230) NCT06225596

Locally advanced or metastatic urothelial carcinoma

A randomized, open-label, phase 2/3 study of Nectin-4–targeting Bicycle® Drug Conjugate zelenectide pevedotin (BT8009) as monotherapy or in combination in patients with locally advanced or metastatic urothelial carcinoma (la/mUC)

Actively recruiting

COHORT 1[1]

1L la/mUC

STRATIFIED BY:
- Cisplatin eligibility
- ± liver metastases
- ECOG PS (0 vs 1/2)

R 1:1:1

- zelenectide pevedotin 5 mg/m² (D1/D8/D15) + pembrolizumab 200 mg (D1) 21-day cycle
- zelenectide pevedotin 6 mg/m² (D1/D8) + pembrolizumab 200 mg (D1) 21-day cycle
- chemotherapy (gemcitabine + cisplatin/carboplatin) ± avelumab maintenance

INTERIM ANALYSIS 1 → Dose selection → zelenectide pevedotin optimal dose + pembrolizumab 200 mg D1 of a 21-day cycle

INTERIM ANALYSIS 2

PRIMARY ANALYSIS

n=956

COHORT 2[1]

2L+ la/mUC

STRATIFIED BY:
- ± prior PD-1/PD-L1 therapy
- ± liver metastases

R 1:1

- zelenectide pevedotin 5 mg/m² (D1/D8/D15) 21-day cycle
- zelenectide pevedotin 6 mg/m² (D1/D8) 21-day cycle
- zelenectide pevedotin optimal dose + pembrolizumab 200 mg D1 of a 21-day cycle

INTERIM ANALYSIS 1 → Dose selection → zelenectide pevedotin optimal dose

PRIMARY ANALYSIS

Primary endpoints[1]:

PFS (cohort 1)
ORR (cohort 2)

Go to **bladdercancerclinicaltrial.com** or contact **duravelo2@bicycletx.com** to enroll patients and learn more.

See eligibility criteria on reverse side.

1L=first line; 2L=second line; D=day; ECOG PS=Eastern Cooperative Oncology Group performance status; ORR=objective response rate; PD-1=programmed cell death protein 1; PD-L1=programmed cell death ligand 1; PFS=progression-free survival.

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Are your patients eligible?

Key eligibility criteria

COHORT 1 (untreated la/mUC)[1]

- ✓ Confirmed la/mUC of the renal pelvis, ureter, bladder, or urethra
- ✓ eGFR ≥30 mL/min
- ✓ ECOG PS ≤2
- ✓ No prior systemic treatment for la/mUC[a] and eligible to receive platinum-based chemotherapy
- ✗ Prior treatment with a CPI for any other malignancy within the last 12 months
- ✗ Uncontrolled diabetes (HbA1c ≥8%)

COHORT 2 (previously treated la/mUC)[1]

- ✓ Confirmed la/mUC of the renal pelvis, ureter, bladder, or urethra
- ✓ Must have received ≥1 prior systemic treatment[b] for la/mUC[c]
- ✓ eGFR ≥30 mL/min
- ✓ ECOG PS ≤1
- ✗ Ongoing Grade ≥2 toxicity associated with prior treatment for UC
- ✗ Prior treatment with EV or any other MMAE-based therapy
- ✗ Uncontrolled diabetes (HbA1c ≥8%)

Additional protocol-defined inclusion/exclusion criteria apply.

The Duravelo-2 study opened in Q1 of 2024. At the most recent data cutoff from Duravelo-1, zelenectide pevedotin demonstrated a tolerable safety profile and preliminary antitumor activity as monotherapy and in combination with pembrolizumab in mUC.[2-5]

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Product candidates are investigational only and are not approved medicines.

[a]Patients with prior neoadjuvant/adjuvant chemotherapy, MMAE-based therapy, and immune checkpoint inhibitor therapy with recurrence >12 months from completion of therapy are allowed.

[b]Including neoadjuvant/adjuvant platinum-based chemotherapy if recurrence occurred <12 months of completing therapy.

[c]The percentage of patients who had received prior PD-1/PD-L1 inhibitor is capped at 50%.[1]

CPI=checkpoint inhibitor; ECOG PS=Eastern Cooperative Oncology Group performance status; eGFR=estimated glomerular filtration rate; EV=enfortumab vedotin; HbA1c=hemoglobin A1C; la/mUC=locally advanced or metastatic urothelial carcinoma; MMAE=monomethyl auristatin E; mUC=metastatic urothelial carcinoma.

References: 1. Loriot Y, et al. Presented at: 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4; Chicago, IL. Abstract TPS4619. **2.** Baldini C, et al. Presented at: 2023 American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL. Abstract 498. **3.** Bader J, et al. Presented at: 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL. Abstract 3088. **4.** Reig Torras O, et al. Presented at: European Society for Medical Oncology (ESMO) Congress 2024; September 13-17, 2024; Barcelona, Spain. Abstract 652P. **5.** Giannatempo P, et al. Abstract presented at 2025 Society of Clinical Oncology (ASCO) Annual Meeting; May 30-June 3; Chicago, IL.

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