

A Phase 1/2 study of detalimogene voraplasamid (EG-70) intravesical monotherapy for patients with high-risk non-muscle invasive bladder cancer (NMIBC)

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Background: High-risk NMIBC is generally treated with adjuvant intravesical bacille Calmette-Guérin (BCG); however, ~50% of patients experience recurrence and/or progression after BCG and are considered unresponsive. Detalimogene voraplasamid (EG-70) is an investigational, intravesically administered therapy designed to elicit local stimulation of anti-tumor immune responses in the bladder and drive durable efficacy in BCG-unresponsive NMIBC, while mitigating the risk of systemic toxicities from immune stimulation. The Phase 1 (dose-escalation) portion of the first-in-human Phase 1/2, open-label, multicenter study (LEGEND; NCT04752722) of detalimogene voraplasamid is complete. The Phase 2 dose was identified, treatment was generally well tolerated, and the overall complete response (CR) rate was 73% [Kalota S, et al. AUA 2024]. Here we describe the ongoing Phase 2 portion of the study, which opened to enrollment in May 2023; a new cohort of papillary only (no carcinoma *in situ* [CIS]) disease is being included.

Methods: Eligibility criteria: age ≥18 years; ECOG PS 0–2; NMIBC, with/without resected coexisting papillary tumors, ineligible for, or elected not to undergo, cystectomy; satisfactory bladder function. Patients receive detalimogene voraplasamid 0.8 mg/mL in 50 mL (intravesical administration, Weeks 1, 2, 5 & 6, 12-week cycle) for 4 cycles: BCG-unresponsive with CIS (Cohort 1); BCG-exposed or BCG-naïve with CIS (Cohort 2); BCG-unresponsive with high-grade papillary bladder cancer without CIS (Cohort 3). Phase 2 primary endpoints: efficacy (CR rate at Week 48); safety. Secondary endpoints: progression-free survival; CR rate at Weeks 12, 24, 36, and 48; duration of response. The study is being conducted in accordance with the ethical principles of the Declaration of Helsinki and is consistent with ICH/GCP. All patients provide written informed consent. The Phase 2 portion of the study is enrolling and will recruit up to 300 patients from sites in the USA, Canada, Europe, and the Asia-Pacific region.