A Phase I/II Study of Detalimogene Voraplasmid Intravesical Monotherapy for Patients with High-Risk Non-Muscle Invasive Bladder Cancer

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Disclosure: This study was funded by enGene. Please click here for a full list of author disclosures.

Keywords: Detalimogene, genetic medicine-based immunotherapy, high-risk non-muscle invasive bladder cancer (NMIBC), LEGEND, Phase I/II study.

Citation: EMJ Urol. 2025;13[1]:36-37. https://doi.org/10.33590/emjurol/SPRE3435

INTRODUCTION AND OBJECTIVES

High-risk, non-muscle-invasive bladder cancer (NMIBC) is generally treated with intravesical Bacille Calmette-Guérin (BCG); however, ~50% of patients experience recurrence and/or progression after BCG and are considered unresponsive.[1] Detalimogene voraplasmid (EG-70) is an investigational, intravesically administered, non-viral gene therapy designed to elicit local stimulation of anti-tumour 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 I portion of the open-label, multicentre LEGEND trial identified the selected dose for Phase II, which was generally well tolerated with an overall complete response (CR) rate of 73%.[2] Here, the authors describe the ongoing Phase II portion of the trial, which is open to enrolment; where a new cohort of papillary-only (no carcinoma *in situ* [CIS]) disease is being included.

MATERIALS AND METHODS

The aim of the single-arm, open-label, Phase II portion of LEGEND (NCT04752722)[3] is to evaluate the efficacy and safety of the identified Phase II dose in patients with high-risk NMIBC. Selected eligibility criteria: age ≥18 years; Eastern Cooperative Oncology Group (ECOG) performance status 0–2; with/without resected coexisting papillary tumours, ineligible for, or elected not to undergo, cystectomy; and satisfactory bladder function. Patients receive detalimogene 0.8 mg/mL in 50 mL by intravesical administration at Weeks 1, 2, 5, and 6 of a 12-week cycle for 4 cycles; patients with CR at the end of the 4th cycle enter maintenance treatment (2 instillations per cycle, at Weeks 1 and 2 for up to 8 cycles)in three cohorts: BCG-unresponsive with CIS ± papillary disease (Cohort 1); BCG-naïve (Cohort 2a) and BCG-exposed

(Cohort 2b) with CIS ± papillary disease; and BCG-unresponsive with high-grade papillary bladder cancer without CIS (Cohort 3).

The Phase II primary endpoints are efficacy (CR rate at Week 48) and safety. Secondary endpoints include: progression free survival; CR rate at Weeks 12, 24, 36, and 96; duration of response; and quality of life. The trial is being conducted in accordance with the ethical principles of the Declaration of Helsinki and is consistent with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) good clinical practice(GCP). All patients provide written informed consent. The ongoing Phase II portion of the trial will recruit up to 300 patients, with sites planned in the USA, Canada, Europe, and the Asia-Pacific region.

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