ABSTRACT #1900 / FPN ESMO CONGRESS 2026 • TRIAL IN PROGRESS • NCT07484022

A phase 1 study of GB-4362, a free MMAE-neutralizing antibody, with enfortumab vedotin and pembrolizumab in advanced urothelial cancer

Generate : Biomedicines℠

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Background

Enfortumab vedotin (EV) plus pembrolizumab is a first-line standard for locally advanced or metastatic urothelial cancer.

Systemic release of monomethyl auristatin E (MMAE) from EV contributes to off-target toxicity. Peripheral neuropathy is a key treatment-limiting toxicity of EV, reported in 67%[a] of patients in EV-302, leading to dose interruption (22%), reduction (13%), or discontinuation (15%); symptoms may persist after treatment and limit the duration and intensity of an otherwise effective regimen.

Therapeutic Concept

GB-4362 is designed to selectively bind and neutralize circulating free MMAE without binding intact EV, with the goal of reducing neuropathy and improving the therapeutic window.

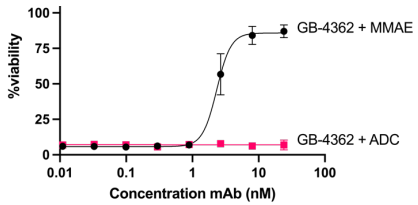
Reducing treatment-related toxicities may help patients remain on EV plus pembrolizumab longer and support broader use across community and other care settings.

Phase 1 data may also inform development of GB-4362 with other MMAE-based antibody-drug conjugates, potentially extending the approach to additional cancer types.

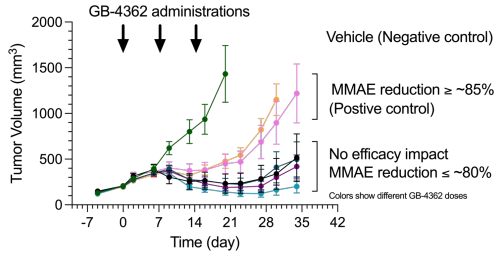
GB-4362 has received Fast Track designation from the U.S. FDA for the prevention and/or reduction of EV-induced toxicity in patients with urothelial cancer.

Preclinical Data

In vitro, GB-4362 blocked MMAE, and not ADC cytotoxicity



In mouse, EV's efficacy was preserved up to 80% MMAE reduction with GB-4362



In monkeys, single dose GB-4362 resulted in dose-dependent reduction in free MMAE which was associated with neutropenia improvement

Treatment	Grade 4 Neutropenia (%)	Free MMAE % (AUC0-2wk)
4mg/kg EV	100%	100%
4mg/kg EV + 0.5mg/kg GB-4362	100%	74%
4mg/kg EV + 2mg/kg GB-4362	50%	52%
4mg/kg EV + 4mg/kg GB-4362	33%	32%

Grade 4 neutropenia is defined as ANC < 0.5 × 10^3 cells/μL. EV = enfortumab vedotin

Dose-escalation study design

Dose Level 1 GB-4362 › **Dose Level 2 GB-4362** › **Dose Level 3 (optional) GB-4362**

DOSE EXPANSION
Preliminary recommended Phase 2 dose of GB-4362

- EV+Pembrolizumab administered per standard of care
- Dose Escalation (6+3 design): GB-4362 only administered in cycles 2-3.
- GB-4362 administered on same days as EV
- Target ~50% MMAE reduction using intra-patient MMAE data

Key eligibility

- **Locally advanced or metastatic urothelial carcinoma** with measurable disease
- Planned to receive **standard of care EV plus pembrolizumab**
- **ECOG 0-1** (escalation); **ECOG 0-2** (expansion)
- No **uncontrolled diabetes**
- No **active untreated CNS metastases**
- No **grade >1 sensory or motor peripheral neuropathy**

Endpoints

Primary:
GB-4362-emergent AEs/SAEs incidence and severity

Secondary:
PK and ADA of GB-4362.
Reduction in free MMAE exposure

Study Status

Recruiting
Multiple active U.S. sites

Disclosure statement: S.F. Funt reports stock or other ownership in Allogene Therapeutics and Doximity; immediate family member's stock or ownership in 76Bio, Urogen Pharma, and Vida Ventures; consulting fees from Daiichi Sanko; and research funding to institution from ALX Oncology, AstraZeneca, Decibel Therapeutics, Genentech/Roche, Generate Biomedicines, and Merck.

No clinical outcome data are presented. Source: ClinicalTrials.gov NCT07484022 (updated 18 Jun 2026) | clinicaltrials@generatebiomedicines.com | +1 617 655 7500

a. PADCEV® (enfortumab vedotin-ejfv) U.S. Prescribing Information. Astellas Pharma US, Inc.; revised Nov 2025. Table 7.

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