Abstract TPS429

A Phase 1 Study of EO-3021 in Adult Patients with Solid Tumors Likely to Express CLDN18.2

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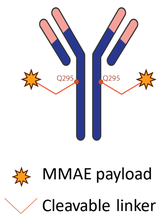
ELEVATION ONCOLOGY

INTRODUCTION

- Claudin 18 isoform 2 (CLDN18.2), a tight junction protein normally expressed only on gastric mucosa, has broad expression in gastric and GEJ, pancreatic, esophageal, and other solid tumors[1]
- EO-3021/SYSA1801 is an antibody drug conjugate (ADC) composed of a mAb targeting CLDN18.2 with a MMAE payload site-specifically conjugated at glutamine 295 (Q295) via a cleavable linker. EO-3021 was designed with a DAR of 2[2] (Fig 1A)
- EO-3021 selectively delivers a potent cytotoxic MMAE payload directly to cancer cells expressing CLDN18.2, exhibits a bystander effect, and retains ADCC and CDC activity[2]
- EO-3021 induced tumor regressions with a single dose across low, medium, and high CLDN18.2-expressing in vivo models and outperformed SOC chemotherapy[2] (Fig 1B)

A. EO-3021 structure



B. NUGC4-CLDN18.2 Gastric Xenograft Model, CLDN18.2 Medium, HER2 Amplified

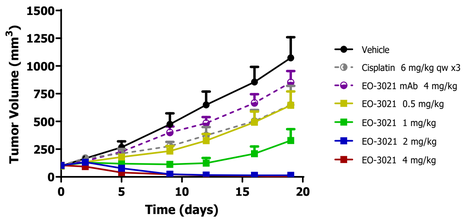


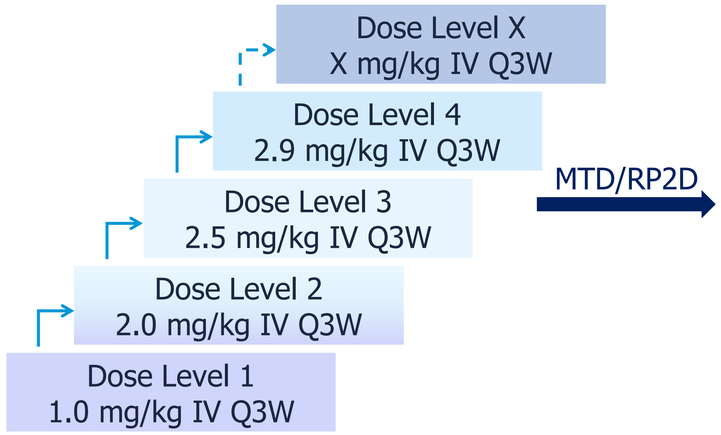
Figure 1. EO-3021 structure (A) and in vivo anti-tumor activity (B)

Abbreviations: ADC, antibody drug conjugate; ADCC, antibody-dependent cellular toxicity; CDC, complement-dependent cytotoxicity; DAR, drug-antibody ratio; ECOG, Eastern Cooperative Oncology Group; GEJ, gastroesophageal junction; IHC, immunohistochemistry; IV, intravenous; mAb, monoclonal antibody; MMAE, monomethyl auristatin E; MTD, maximum tolerated dose; PK, pharmacokinetics; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended phase 2 dose; SOC, standard of care

METHODS

- This is a Phase 1, open-label, multi-center, dose escalation and expansion study to investigate the safety, tolerability, PK and preliminary anti-tumor activity of EO-3021 in patients with solid tumors likely to express CLDN18.2
- Key Inclusion Criteria:
  - Adult patients (age ≥18 years) with histologically and/or cytologically confirmed diagnosis of advanced unresectable or metastatic solid tumor that is likely to express CLDN18.2 such as gastric cancer/GEJ, pancreatic, esophageal cancer
  - ECOG performance status 0 or 1 at screening
  - Progressed on or after standard therapy, or are intolerable for available standard therapy, or there is no available standard therapy
  - At least one measurable extra-cranial lesion as defined by RECIST v1.1
- Key Exclusion Criteria:
  - Have previously received CLDN18.2 ADC or any ADC containing an auristatin payload (prior monoclonal antibody against CLDN18.2 may be eligible)
  - Have peripheral neuropathy Grade ≥2
- Expression of CLDN18.2 is not required; tumor samples will be collected for retrospective assessment of CLDN18.2 by IHC
- Dosing: Patients will receive EO-3021 IV once every three weeks (Q3W) until disease progression or unacceptable toxicity

Part A: Dose Escalation



Part B: Expansion

Gastric/GEJ adenocarcinoma

- Patients with advanced unresectable or metastatic gastric/GEJ adenocarcinoma will receive EO-3021 IV infusion Q3W until disease progression or unacceptable toxicity

Primary Objectives

- Determine the single-agent EO-3021 RP2D and schedule for further exploration in patients with advanced solid tumors that are likely to express CLDN18.2

Secondary Objectives

- Safety profile, PK profile, immunogenicity and early indication of clinical efficacy of EO-3021

TRIAL STATUS

- Enrollment in the dose escalation portion of the study began in August 2023
- For additional information on actively enrolling sites, please refer to www.clinicaltrials.gov (NCT05980416)
- This study is sponsored by Elevation Oncology, Inc.

REFERENCES

1. Sahin U, et al. Clin Cancer Res. 14(23), 2008
2. Dan M, et al. Cancer Res. 83, 2023

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