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Phase 1b Study of Zocilurtatug Pelitecan in Patients with Advanced Extra-Pulmonary Neuroendocrine Carcinomas

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BACKGROUND

Extra-pulmonary neuroendocrine carcinomas (epNECs) are aggressive malignancies with poor prognosis and limited treatment options following platinum-based chemotherapy. Delta-like ligand 3 (DLL3) is broadly expressed in neuroendocrine cancers and minimally expressed in normal tissues, making it an attractive therapeutic target. Zocilurtatug Pelitecan (Zoci, formerly known as ZL-1310) is a novel DLL3-targeted antibody-drug conjugate (ADC) utilizing the TMALIN® platform targeting DLL3-expressing tumor cells.

METHODS

This open-label, multicenter Phase 1b study enrolled patients with advanced or metastatic epNEC who progressed on or after platinum-based chemotherapy. Zoci was administered intravenously at 1.6 mg/kg every 3 weeks until disease progression or unacceptable toxicity. Investigator-assessed tumor responses were evaluated by RECIST v1.1 (and PCWG3 for neuroendocrine prostate cancer). DLL3 expression was assessed retrospectively via immunohistochemistry (IHC) using H-score analysis. The data cutoff date was February 18, 2026.

RESULTS

A total of 46 patients in Phase 1b were dosed. Among the modified response evaluable set (n=34), 53% (18/34) had gastroenteropancreatic neuroendocrine carcinoma (GEP-NEC)

and 47% (16/34) had non-GEP NEC. The median number of prior systemic therapy lines was 1. The confirmed objective response rate (ORR) was 38.2% (13/34), and the overall disease control rate was 55.9% (19/34). Tumor reduction was observed across a diverse range of epNEC primary tumor types. Because of limited follow-up, progression-free survival and duration of response remained immature. Across the total safety population (n=46), 97.8% of patients experienced a treatment-emergent adverse event (TEAE), and grade ≥ 3 TEAEs occurred in 30.4% of patients. DLL3 expression, measured by H-score, were obtained in 31 efficacy evaluable patients, with 80.6% (25/31) being positive. The median H-score was 133. The ORR was 50.0% (8/16) in patients with DLL3 H-scores above the median, compared with 26.7% (4/15) in those expressing below the median. However, preliminary analyses did not reveal a definitive association between DLL3 expression and ORR.

CONCLUSIONS

Zoci demonstrates clinically meaningful responses and a manageable safety profile in heavily pretreated patients with epNECs. The frequency and severity of adverse events were consistent with previous clinical experience, establishing a preliminary favorable benefit-risk profile in this population. Responses were observed across a range of expression levels. With the Phase 1b portion complete, the study has expanded into Phase 2 to further evaluate the durability of response and clinical efficacy. Updated data, including durability of response, will be presented.

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