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A Phase 2 Open-Label Study of Belzutifan (a HIF-2α Inhibitor) Monotherapy in Patients with Advanced/Metastatic Pheochromocytoma/ Paraganglioma or Pancreatic Neuroendocrine Tumors

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BACKGROUND

Patients with advanced pheochromocytoma/paraganglioma (PPGL) or pancreatic neuroendocrine tumor (panNET) are in need of novel targeted therapies. Hypoxia-inducible factor 2α (HIF-2α) is one of the key oncogenic drivers in neuroendocrine tumors. Hypoxia signaling pathway alterations or other mechanisms that stabilize HIFs are common in some PPGLs and panNETs. Belzutifan (MK-6482), a HIF-2α inhibitor, has shown antitumor activity in advanced renal cell carcinoma and localized von Hippel-Lindau (VHL) disease–associated tumors, including panNETs. The current phase 2 study (NCT04924075) will evaluate the efficacy and safety of belzutifan in patients with advanced PPGLs or panNETs.

METHODS

This open-label, multicenter, single-arm, phase 2 study is enrolling patients aged ≥12 years (body weight ≥40 kg if aged 12–17 years) with histopathologically documented, unresectable, locally advanced/metastatic PPGLs (BP ≤150/90 mmHg [≤135/85 mmHg if adolescent]) (cohort A1) or histopathologically documented, advanced/metastatic well-differentiated G1/G2 (2017 WHO criteria) panNETs with progression on prior targeted therapy (cohort A2). Other eligibility criteria include progressive disease (PD) ≤12 months from screening, measurable disease per RECIST v1.1 by blinded independent central review (BICR), ECOG PS ≤1, and archival/new tumor sample for biomarker analysis. Approximately 140 patients (70/cohort) will be enrolled and receive belzutifan 120 mg once daily until PD or unacceptable toxicity. Tumor imaging occurs initially at week 9, then every 8 weeks through week 49, and every 12 weeks thereafter.

The primary study endpoint is objective response rate per RECIST v1.1 by BICR. Secondary endpoints are duration of response, time to treatment response, disease control rate, progression-free survival, overall survival, and safety. Enrollment began in August 2021, and is ongoing at 44 international sites.

RESULTS

N/A

CONCLUSIONS

N/A

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