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Phase 2 Study of Targeted Alpha Therapy ²¹²Pb-DOTAMTATE in Patients with Advanced Gastroenteropancreatic (GEP)-NETs Previously Treated with PRRT

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BACKGROUND

Effective treatment options are limited for patients with unresectable or metastatic Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs) whose disease progresses after peptide receptor radionuclide therapy (PRRT) with beta-emitting ¹⁷⁷Lu-labelled somatostatin analogs (SSA). ²¹²Pb-DOTAMTATE (SAR447873) is a novel SSTR-targeted alpha therapy under clinical evaluation for patients with SSTR+ NETs in a Phase 2 two-cohort trial (ALPHAMEDIX 02 [NCT05153772]). In PRRT-naïve patients (cohort 1), treatment was associated with a 54.3% overall response rate (ORR) and a manageable safety profile. Here we report the first efficacy and safety results in patients previously treated with PRRT (cohort 2).

METHODS

This is a Phase 2, open-label, multicenter study evaluating the clinical activity of ²¹²Pb-DOTAMTATE in PRRT-naïve and PRRT-exposed patients with histologically confirmed unresectable or metastatic GEP-NETs, positive SSA imaging and at least 1 site of measurable disease. PRRT-exposed patients had progressive disease after receiving ≤4 doses of ¹⁷⁷Lu-SSA and received their last dose ≥6 months prior to Day 1. ²¹²Pb-DOTAMTATE was administered at 67.6 μCi/kg every 8 weeks for up to 4 cycles. Primary endpoints include ORR per RECIST1.1, and safety. Secondary endpoints include progression free survival and overall survival.

RESULTS

Among 26 PRRT-exposed patients, the most common primary tumor sites were pancreas and small intestine (both n=11, 42.3%). The majority (n=20; 76.9%) had Grade 1/2 tumors. Eight patients (30.8%) achieved a confirmed partial response (PR); 17 (65.4%), stable disease (with 1 unconfirmed PR pending confirmation); and 1 (3.8%), progressive disease (96.2% disease control rate). Seven of 8 patients with a confirmed PR maintained their response at the time of data cutoff. All patients experienced at least one treatment-emergent adverse event (TEAE), with 9 (34.6%) having at least one Grade ≥3 TEAE. The most common Grade 3 or 4 TEAE was lymphocyte count decrease (15.4%).

CONCLUSIONS

In patients with unresectable or metastatic SSTR+ GEP-NETs previously treated with PRRT,²¹²Pb-DOTAMTATE (SAR447873) was associated with a clinically meaningful overall response rate of 30.8%. TEAEs were generally Grade 1 or 2 and manageable.

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