C-15

Long-term Follow-up of PRRT-Naïve Patients with GEP-NETs Treated with Targeted Alpha Therapy 212Pb-DOTAMTATE in the Phase 2 ALPHAMEDIX 02 Trial

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BACKGROUND

Alpha-emitting radioisotopes efficiently induce double-stranded DNA breaks in tumors while aiming to spare healthy tissue, given their high linear energy transfer over short ranges. ^{212}Pb-DOTAMTATE (SAR447873) is a novel somatostatin receptor (SSTR)-targeted alpha therapy under clinical evaluation for patients with unresectable or metastatic SSTR+ gastroenteropancreatic neuroendocrine tumors (GEP-NETs) (ALPHAMEDIX 02 [NCT05153772]). Here we present a two-year landmark analysis of the efficacy and safety of ^{212}Pb-DOTAMTATE in patients with no prior exposure to peptide receptor radionuclide therapy (PRRT).

METHODS

ALPHAMEDIX 02 is a Phase 2, open-label, multicenter study evaluating the efficacy, safety, and tolerability of ^{212}Pb-DOTAMTATE in PRRT-naïve (cohort 1, N=35) and PRRT-exposed (cohort 2, N = 26) patients with histologically confirmed unresectable or metastatic GEP-NETs, positive somatostatin analogue imaging and at least 1 site of measurable disease. ^{212}Pb-DOTAMTATE was administered at 67.6 µCi/kg every 8 weeks for up to 4 cycles. Primary endpoints include ORR per RECIST1.1, and incidence and severity of adverse events (AEs). Secondary endpoints include progression free survival (PFS) and overall survival (OS).

RESULTS

As of 14 April, among 35 PRRT-naïve patients, the most common primary tumor sites were pancreas and small intestine (both n=15, 42.9%). The majority (n=31, 88.6%) had Grade 1/2 tumors. Twenty patients achieved a confirmed partial response (ORR 57.1%; 95% CI: 39.4–73.7); 13 (37.1%), stable disease; and 1 (2.9%), progressive disease (1 patient not evaluable). Fourteen of 20 patients with a confirmed response had a duration of response (DOR) ≥12 months; 2 patients had a DOR ≥24 months. Two-year PFS and OS rates were 71.3% and 88.2%, respectively. All patients experienced ≥1 treatment-emergent adverse event (TEAE). The most common Grade 3 or 4 TEAE was decreased lymphocyte count (25.7%).

CONCLUSIONS

With 2 years median follow-up, ^{212}Pb-DOTAMTATE (SAR447873) treatment continues to be associated with frequent, durable responses and survival in patients with advanced SSTR+ GEP-NETs. No new safety signals emerged with longer follow-up.

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