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Targeted Alpha Therapy with 212Pb-DOTAMTATE in subjects with advanced somatostatin receptor-expressing gastroenteropancreatic neuroendocrine tumors

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BACKGROUND

^{212}Pb-DOTAMTATE is a Targeted Alpha Therapy (TAT) in clinical development for subjects with SSTR+NETS. A Phase 1 dose-escalation study has already been completed. TAT holds the promise to improve outcomes versus Peptide Receptor Radionuclide Therapy (PRRT) with beta-emitters like ^{177}Lu-DOTATATE, currently considered standard of care for subjects with GEP-NETs.

METHODS

ALPHAMEDIX 02 is a Phase 2, open-label, multicenter study evaluating safety, tolerability and efficacy of ^{212}Pb-DOTAMTATE in PRRT-naïve (Cohort 1, N = 35) and PRRT-refractory (Cohort 2, N = 26) subjects with histologically confirmed unresectable or metastatic GEP-NETs, positive SSTR imaging and at least 1 site of measurable disease per RECIST 1.1. ^{212}Pb-DOTAMTATE was administered at 67.6 µCi/kg per cycle, every 8 weeks, for up to 4 cycles. Primary endpoints include overall response rate (ORR) per RECIST1.1, and incidence and severity of adverse events (AEs). Secondary endpoints include progression free survival, overall survival, and health-related quality of life. Initial results of the already completed Cohort 1 are presented.

RESULTS

In Cohort 1, 19 out of 35 subjects with metastatic SSTR+ GEP-NETs achieved a confirmed response (ORR 54.3% (95%CI: 38.2-69.5%)). In the Phase 1 trial, five out of eight PRRT-naïve subjects with SSTR+ GEP-NETs treated with the same regimen of ^{212}Pb-DOTAMTATE achieved a response (ORR 62.5% (30.6-86.3%)): the combined ORR from both studies is 55.8% (41.1-69.6%). Median Duration of Response (DOR) has not been reached in either study. Four out of four subjects (100%) with confirmed response in Phase 1 had a DOR of ≥ 12 months. In the ongoing Phase 2 study: so far 19 out of 19 subjects (100%) with confirmed response had a DOR of ≥ 6 months, and 10 out of 11 (91%) had a DOR of ≥ 12 months. Lymphocytopenia is a main cause of the 60% Grade 3 and 4 AEs reported overall in Cohort 1. Three deaths were reported as fatal AEs: underlying progressive disease (N = 2) and multiorgan failure/sepsis (N=1)

CONCLUSIONS

In PRRT-naïve subjects with SSTR+ unresectable or metastatic GEP-NETs, treatment with ^{212}Pb-DOTAMTATE was well-tolerated, with a safety profile consistent with the underlying disease and expected toxicities of radioligand therapy, similar to ^{177}Lu-DOTATATE. The 54.3% ORR in Cohort 1 (55.8% in pooled dataset) appears to be substantially higher than the ORR previously reported for ^{177}Lu-DOTATATE in the pivotal NETTER-1 study (18% (10–25%)).

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