# C-19

## [212Pb]VMT-alpha-NET for advanced SSTR+ NETs: safety and preliminary efficacy results from cohorts 1 and 2 of the dose escalation phase

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### BACKGROUND

Somatostatin receptor subtype 2 (SSTR2) is expressed in neuroendocrine tumors (NETs), and it is an important target for both diagnosis and therapy. [$^{212}$Pb]VMT-alpha-NET is an alpha therapy agent targeting SSTR2-expressing NETs. Here, we report the results of a prospective, open-label, Phase I/IIa clinical trial evaluating the safety, tolerability, pharmacokinetics, and preliminary efficacy of [$^{212}$Pb]VMT-alpha-NET [NCT05636618].

### METHODS

Adults with well-differentiated unresectable or metastatic SSTR2-expressing NETs, who are peptide receptor radionuclide therapy (PRRT) naïve, and who progressed on at least one prior line of systemic therapy, are eligible. The study design follows a Bayesian dose-finding algorithm. Participants receive up to four doses of [$^{212}$Pb]VMT-alpha-NET on 8-weeks intervals at the assigned dose level. Efficacy is assessed by investigators according to RECIST criteria v1.1.

### RESULTS

As of 30-Apr-2025, nine participants were enrolled for dose-limiting toxicity (DLT) observation into cohort 1 (n=2) and cohort 2 (n=7) at dose levels of 92.5 MBq [2.5 mCi] and 185 MBq [5 mCi], respectively. Thirty-three (33) additional patients were enrolled into cohort 2 to further evaluate safety and efficacy at the selected dose. Safety was assessed for all participants treated (n=42), while efficacy was evaluated for the nine participants enrolled for DLT-observation. Among all participants treated with [$^{212}$Pb]VMT-alpha-NET (n=42), no DLTs, no grade 4 or 5 adverse events (AEs), no treatment-related discontinuations, no serious renal complications or myelosuppression, and no dysphagia were observed. Four out of seven participants (57%) enrolled for DLT-observation in cohort 2 achieved an objective response with a median follow-up time of 52 weeks (range: 6,64). Three objective responses were confirmed, while one was pending confirmation at the time of data cut-off (DCO). Overall, seven of the nine participants (78%) enrolled for DLT-observation both in cohort 1 and 2 were without progression as of the DCO, with a median follow up time of 56 weeks (range: 6,77). Cohort 3, at a dose level of 222 MBq [6 mCi], has recently been opened for enrollment. Safety data for all treated participants and efficacy results for a mature subset will be presented at the congress.

## CONCLUSIONS

[$^{212}$Pb]VMT-alpha-NET is a well-tolerated therapy for patients with advanced NETs, and it has shown promising clinical benefit at the dose level of 185 MBq [5 mCi]. The study is ongoing and open for enrollment in cohort 3.

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