Title: Real-World Outcomes of Patients with Bronchopulmonary Neuroendocrine Tumors treated with Lutetium Lu-177 DOTATATE: An updated multi-institution cohort

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Background: Bronchopulmonary neuroendocrine tumors (BPNETs) comprise an estimated 20-30% of all neuroendocrine tumors (NETs). Management of metastatic BPNETs remains largely individualized, with lutetium-177 (^{177}Lu) DOTATATE, a peptide receptor radionuclide therapy (PRRT), emerging as a promising treatment in NETs with selective targeting of somatostatin receptor expressing cells. Here, we present real-world utilization and outcome data of PRRT in BPNETs.

Methods: We conducted a retrospective analysis of patients with metastatic BPNETs treated at Mayo Clinic sites (AZ/FL/MN) with PRRT between 2014 and 2025. Patients were identified via institutional records and confirmed using the Mayo Data Explorer platform. Tumor grade and histology were defined by Ki-67 and per WHO 2017 criteria, respectively. Treatment response was assessed by 3-month post-treatment interval restaging imaging and clinician assessment. Progression free survival (PFS) defined as time from PRRT initiation to any disease progression, death or last follow up. Overall survival (OS) was defined as time from PRRT initiation to death or last known follow up. Statistical analyses were performed with Stata 18.0. Analysis to be updated with additional records across multiple institutions.

Results:
Twenty-three patients [median age 66] were included [14 (61%) males]. Eleven patients had active or former tobacco use with 33 average pack-years. Grade 1, 2, and 3 tumors were seen in 26% (n=6), 39% (n=9) and 26% (n=6) patients, respectively. Histologically, 10 patients had typical carcinoid while 13 had atypical carcinoid. Seven patients (30%) reported functional carcinoid syndrome. Most frequent sites of metastasis were liver (78%, n=18), bone (61%, n=14), pancreas (9%, n=2) and contralateral lung (4%, n=1). Majority of patients had Krenning score-4 (57%), followed by score-3 (30%), and score-2 (13%). PRRT was most commonly administered as third-line systemic therapy (52%), followed by fourth-line (22%), second-line (17%), and later-lines (9%). Preceding cancer-directed therapies included somatostatin analogs (100%), systemic chemotherapy (65%; 10/15 single-line, 5/15 multiple-lines; 8/15 platinum/etoposide, 4/15 capecitabine-temozolomide), everolimus (43%), and tyrosine kinase inhibitor (9%). 17/23 (74%) patients received 4 doses PRRT (median 4, range 2-6). No patient had complete response; partial response was observed in 17% (4/23), stable disease in 30% (8/23), progressive disease in 43% (9/23). Most common adverse events included fatigue (35%), nausea (26%), abdominal pain (22%), and decreased appetite (13%); no events ≥ grade 3 were reported. Median PFS was 10.8 months (95% CI: 7.3-15.9). In subgroup analysis, median PFS by Krenning score 4 vs. ≤3 was 14.7 vs. 7.3 months (p=0.042). By histology, median PFS for typical vs. atypical tumors was 11.1 vs. 8.4 months (p=0.463). Median OS was 35.6 months (95% CI:11.9-50.2) with 9/23 (39%) patients alive at time of data collection. Following PRRT, 10/23 (43%) patients received no further treatment, with 4/23 (17%) receiving 1 additional line and 7/23 (30%) receiving ≥2 lines.

Conclusion: In this retrospective analysis of patients with metastatic BPNETS, lutetium (^{177}Lu) DOTATATE demonstrated a response rate of 17%, disease control rate of 48%, and a median PFS of 10.8 months. In clinical practice, decision of when to utilize PRRT varies widely, found here most commonly as a 3rd line systemic agent.