Evaluation of DOTATATE-PET After Two Cycles of Peptide Receptor Radionuclide Therapy (PRRT) in Neuroendocrine Tumors (NETs)

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Background

Well-differentiated NETs overexpress somatostatin receptors (SSTR), which can be targeted for molecular imaging with ^{68}Ga/^{67}Cu DOTATATE PET and treatment with peptide receptor radionuclide therapy (PRRT). We aimed to evaluate the feasibility of DOTATATE-PET after two cycles of PRRT for early treatment response assessment in patients with SSTR-expressing NETs. Additionally, we correlated change of the tumor marker chromogranin A after two treatment cycles to treatment response.

Materials and Methods

In this retrospective study, 120 patients (62 women, 58 men; mean age 61.9±11.1 [54 – 68] years) with histologically verified G1-G3 SSTR-expressing NETs were included. All patients had DOTATATE-PET (PET/CT or PET/MRI), at baseline, after two cycles, and upon completion of PRRT. RECIST v.1.1 and change in SSTR-density (Krenning score) were used to evaluate the scans and assess treatment response. The change in tumor marker chromogranin A was recorded. Patients were surveyed regarding the additional scan midway through the treatment.

Treatment response after 2 PRRT cycles

Response category	DOTATATE-PET *n* (%)
Complete response	0 (0%)
Partial response	58 (48%)
Stable disease	49 (41%)
Progressive disease	4 (3%)
Pseudo-progression	9 (8%)

Pseudo-progression after 2 PRRT cycles

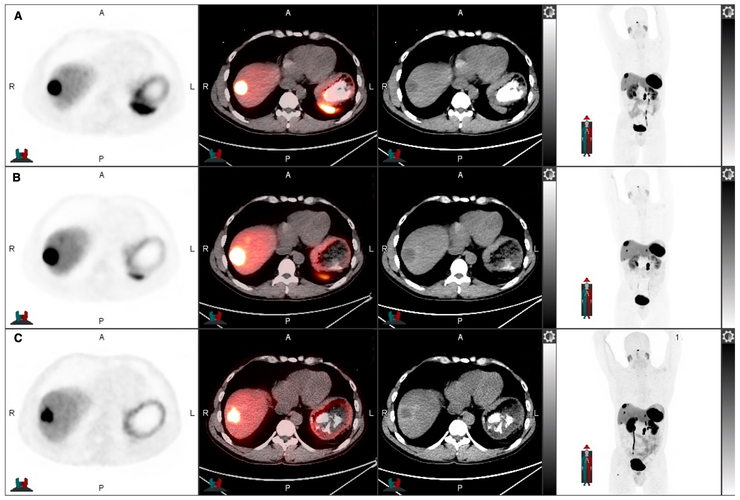

Figure: 45-year-old man with progressive, metastatic pancreatic NET, G3.
At baseline, the index lesion in the liver measures 2.6x2.5 cm in the right dome (A, axial ^{68}Ga-DOTATATE PET, axial fused PET/CT, axial CT, and maximum intensity projection [MIP], respectively). After two PRRT cycles, the lesion shows a size increase to 3.0x2.8 cm with stable SSTR expression, which was considered pseudo-progression (B, axial ^{68}Ga-DOTATATE PET, axial fused PET/CT, axial CT, and MIP, respectively). In the posttreatment PET, a size decrease is noted with 2.3x2.5 cm as sign of treatment response (C, axial ^{64}Cu-DOTATATE PET, axial fused PET/CT, axial CT, and MIP, respectively).

Results

All patients considered additional DOTATATE-PET contributing to their quality of life as it provided reassurance regarding treatment response.
According to RECIST v1.1, progressive disease (PD) was seen in 13/120 (11%) patients. Evaluation of SSTR-density showed true PD in only 4/13 (overall 3%) participants. Follow-up imaging after completion of PRRT showed further PD and proved true PD in these patients.
Patients considered to have pseudo-progression (PSP) showed an overall size increase of up to 3 mm in known NET lesions, with/without central necrosis or new stranding, but no new lesions. Posttreatment DOTATATE-PET was available in 7/9 patients and verified PSP (3/7 PR, 4/7 SD). One patient is still in treatment while one patient passed due to COVID-19.
Chromogranin A was available in 61/120 (51%) patients. The change in chromogranin A between baseline and two PRRT cycles was not positively correlated with response to treatment in PET (r=0.16, P=0.20) or from mid-treatment to post-treatment (r=0.11, P=0.47).

Conclusion

Our data show that DOTATATE-PET after two PRRT cycles is feasible for early treatment response assessment. Image assessment based on the Krenning score is more accurate in distinguishing true PD from PSP than RECIST v1.1, allowing continuation of PRRT in patients with PSP while patients with true PD may be switched to other systemic treatments.
Change in tumor marker chromogranin A did not correlate with response to treatment.