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Role of genetic alterations and tumor functionality in predicting peptide receptor radionuclide therapy effectiveness and survival in pancreatic neuroendocrine neoplasm

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BACKGROUND

Studies exploring the potential of genetic alterations and tumor functionality to predict treatment effectiveness and survival outcome in pancreatic neuroendocrine neoplasm (PNEN) are limited. The objective of this study was to report on the genetic and functional tumor profiles, as well as to examine their association with peptide receptor radionuclide therapy (PRRT) treatment effectiveness and survival outcome in PNEN patients.

METHODS

Patients diagnosed with PNEN seen at Cedars-Sinai were identified. Data of race, ethnicity, tumor functionality, genetic testing results were collected retrospectively. The incidence of genetic alterations and functioning tumors were reported. Progression-free survival (PFS) for evaluating PRRT effectiveness was calculated for patients who received PRRT (n=28) while overall survival (OS) was calculated for the entire patient cohort (n=115). They were compared across groups stratified by somatic mutations, germline mutations, tumor functionality and PRRT treatment status.

RESULTS

Of 115 PNEN patients, 60 had somatic testing results and 49 had germline testing results. Somatic variants were detected in 73.3% of patients (44/60). The most common somatic variants detected were MEN1(33.3%, 20/60), DAXX(18.3%, 11/60), CDKN2A(15.0%, 9/60), ATRX(11.7%, 7/60), CDKN2B(10.0%, 6/60) and TP53(8.3%, 5/60). Germline variants were detected in 20.4% of patients (10/49). The most frequently detected germline variant was APC (6.1%, 3/49). The most common functioning tumors were gastrinoma (9.6%, 11/115) and insulinoma (7.0%, 8/115). Shorter median PFS was associated with the presence of MEN1 (5.4 months), CDKN2A (9.1 months) and CDKN2B (3.0 months) mutations. Longer median OS was noted in ATRX (114.3 months), CDKN2A (78.0 months), CDKN2B (78.0 months) and DAXX (78.0 months) mutations while shorter median OS was noted in MEN1 (47.3 months) and TP53 (9.1 months) mutations. Longer median PFS (16.9 months) and median OS (69.3 months) were noted in patients with functioning tumors.

PFS/OS of PNEN

		Median PFS (months)	Median OS (months)	N (PFS/OS)
Somatic mutations	ATRX	0.9	114.3	3/7
	CDKN2A	9.1	78.0	6/9
	CDKN2B	3.0	78.0	5/6
	DAXX	18.4	78.0	5/11
	TP53	N/A	9.1	0/5
	MEN1	5.4	47.3	6/20
	Without somatic mu-tations	18.0	58.5	6/20
Tumor functionali-ty	Functioning	16.9	69.3	8/23
	Non-functioning	13.8	33.5	20/92

PFS of ATRX/TP53 was not described due to small sample size.

CONCLUSIONS

The findings suggested that genetic alterations and tumor functionality could provide insights into predicting PRRT treatment effectiveness and survival outcome in PNEN patients. The incorporation of genetic and functional tumor profiling could potentially aid in better PNEN management. Further studies with larger sample sizes are needed to enhance the reliability of these results.

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