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

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01. 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
  - to examine their association with peptide receptor radionuclide therapy (PRRT) treatment effectiveness and survival outcome in PNEN patients

02. Methods

Retrospective collection of clinical data for patients diagnosed with PNEN seen at Cedars-Sinai:

- **Race**
- **Ethnicity**
- **Tumor functionality**
- **Somatic mutations**
- **Germline mutations**

Evaluation of PRRT effectiveness and survival outcome:

- **Calculation of progression-free survival (PFS) for patients who received PRRT (n=28)**
- **Calculation of overall survival (OS) for the entire patient cohort (n=115)**
- **Comparison of PFS and OS across groups stratified by**
  - **somatic mutations**
  - **germline mutations**
  - **tumor functionality**
  - **PRRT treatment status**

03. 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.**
- **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.**

Figure 1. Somatic mutations of PNEN patients

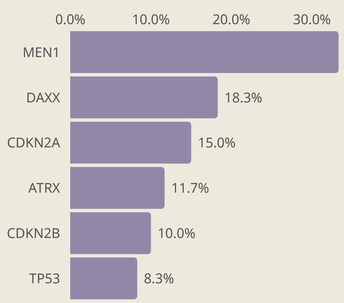

Figure 2. Tumor functionality of PNEN patients

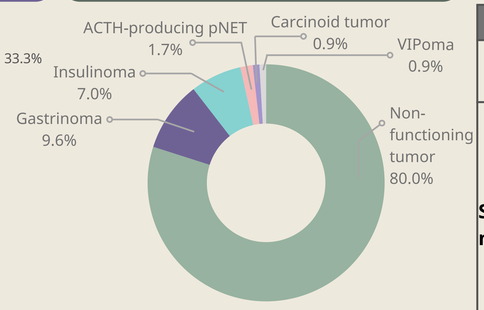

Figure 3. Germline mutations of PNEN patients

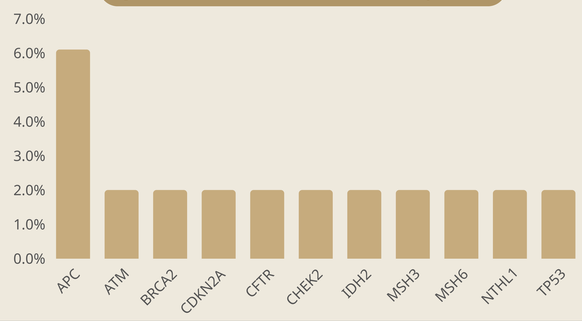

Table 1. PFS and OS of PNEN patients

		Median PFS (months)	N (PFS)	Median OS (months)	N (OS)
Somatic mutations	ATRX	0.9	3	114.3	7
	CDKN2A	9.1	6	78.0	9
	CDKN2B	3.0	5	78.0	6
	DAXX	18.4	5	78.0	11
	TP53	N/A	0	9.1	5
	MEN1	5.4	6	47.3	20
	Without somatic mutations	18.0	10	58.5	16
Germline mutations	APC	0.9	1	24.6	3
	Without germline mutations	14.2	12	25.5	39
Tumor functionality	Functioning	16.9	8	69.3	23
	Gastrinoma	37.0	4	41.2	11
	Insulinoma	7.3	2	54.8	8
	Non-functioning	13.8	20	33.5	92

04. Conclusion

- 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.

05. References

1. Gujarathi R, Abou Azar S, Tobias J, et al. MEN1/DAXX/ATRX mutations enhance progression-free survival in gastroenteropancreatic neuroendocrine tumors treated with peptide receptor radionuclide therapy. Endocr Relat Cancer. 2024;31(11):e240065. Published 2024 Oct 4. doi:10.1530/ERC-24-0065
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