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Response After Neoadjuvant Therapy for Pancreatic Neuroendocrine Tumors

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BACKGROUND

Neoadjuvant therapy (NAT) has been widely employed in PDAC to downsize tumors. However, data to support the routine use of NAT in advanced PNET is limited. This study aims to investigate the objective response rate (ORR) of cytotoxic NAT in advanced PNET.

METHODS

We performed a retrospective review of patients with PNETs who underwent cytotoxic NAT followed by surgical resection at a high-volume tertiary cancer center from January 2009 to August 2023. Demographic and clinicopathologic characteristics were evaluated. ORR was defined as $\geq 30\%$ reduction in serum Chromogranin A (CgA) or hormone level in functional-PNET, partial radiographic response per RESIST v1.1 criteria, and/or tumor downgrading after NAT. Secondary endpoints were progression free survival (PFS) and overall survival (OS).

RESULTS

This cohort of 34 patients had a median follow-up of 42 months (IQR 18–99). 25 (74%) patients had metastatic disease at presentation (Table 1). 26 (76%) patients received neoadjuvant CAPTEM, 2 (6%) received Everolimus, 2 (6%) received Etoposide+Cisplatin, 2 (6%) received Streptozotocin+5-FU+Leucovorin, 1 (3%) received Sunitinib, and 1 (3%) received Evacizumab.

23 (68%) underwent resection of all visible lesions. 11 (32%) underwent cytoreductive surgery with $>70\%$ debulking. 18 (53%) had progression of disease after resection with a median PFS of 33 months (IQR 5–43). Median OS of the cohort was not reached. 3 (9%) patients died due to disease (median resection to death was 58 months). ORR after NAT for the entire cohort was 76% (26 patients). 20 (59%) showed a response by serum biomarker, 10 (29%) by reduction in tumor grade, and 9 (26%) by RESIST criteria. 4 (12%) patients showed response by all 3 criteria; they all received CAPTEM.

Table 1. Study Cohort Demographic and Clinicopathological Characteristics

Cohort Characteristics	N=34(%)
Median Age, yrs(IQR)	56(45-63)
Sex	
Male	15(44%)
Female	19(56%)
Race	
White	31(91%)
Black	2(6%)
Other	1(3%)
Ethnicity	
Hispanic	32(94%)
Non-Hispanic	2(6%)
Tumor Grade	
G1	8(23%)
G2	21(62%)
G3	5(15%)
Surgical Procedure for primary tumor	
Distal Pancreatectomy	21(62%)
Pancreatoduodenectomy	9(26%)
Total Pancreatectomy	4(12%)
Median largest primary tumor Size, cm(IQR)	5.0(3.4-8.0)
Primary Tumor Margin	
RO	23(68%)
R1	11(32%)
Nodal Metastasis	
NO	11(32%)
N1	23(68%)
Distant Metastasis	
M0	9(26%)
M1	25(74%)
Liver	20(59%)
Multiple sites	5(15%)
Neoadjuvant Cytotoxic Regimen	26(76%)
CAPTEM	2(6%)
Streptozotocin, 5-FU, Leucovorin	2(6%)
Everolimus	1(3%)
Evacizumab	1(3%)
Sunitinib	2(6%)
Etoposide, Cisplatin	

CONCLUSIONS

For advanced PNETs, NAT was associated with an ORR of 76%. NAT allowed for surgical resection in patients with advanced metastatic disease and provided durable PFS and OS.

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