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Clinical characteristics and molecular profiling of patients with pancreatic mixed acinar-neuroendocrine carcinoma

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BACKGROUND

Pancreatic acinar cell carcinoma (PACC) is a rare cancer, comprising less than 1% of all pancreatic cancers and often presents as a mixed malignancy with a neuroendocrine component. Limited data exists on its clinical and molecular characteristics. This retrospective study aims to provide additional insights to better understand and characterize the disease.

METHODS

Patients from the Mayo Clinic with pathology records denoting pancreatic acinar cell carcinoma from years 2002 to 2023 were selected for retrospective review. Demographic data, pathologic information, treatment courses, and next generation sequencing (NGS) when available, were collected.

RESULTS

A total of 54 patients (pts) were identified (78% male, n = 42). Median age was 63 years old (range 23-88). Histologic subtypes were 70% pure acinar cell carcinoma (n = 38), 24% mixed acinar-neuroendocrine (n = 13), and 6% mixed acinar-adenocarcinoma (n = 3). At diagnosis, 46% presented with metastatic disease (n = 25), 19% were locally advanced (n = 10), and 35% were resectable (n = 19). Early stages were more likely to undergo upfront surgical resection (84%, n = 16), while locally advanced cancers were frequently treated with neoadjuvant chemotherapy (70%, n = 7) followed by surgical resection (60%, n = 6). FOLFIRINOX was chosen as neoadjuvant therapy in 71% of pts (n = 10), while others received gemcitabine-based therapies. 14 pts had somatic and germline NGS (Table 1) with the following (n = 12 with targetable mutations): homologous recombination (HR) gene alterations (n = 6, 3 treated with olaparib), RAF alterations (n = 6, 2 treated with dabrafenib plus trametinib and 1 with ulixertinib), mismatch repair (MMR) gene alterations (n = 3, 1 treated with pembrolizumab), and *NTRK* alteration (n = 1, ongoing treatment with larotrectinib, 15 months partial response).

Targetable Somatic Alterations (n = 14)	*Germline Testing Results (n = 14)*
HR alterations (n = 6 pts): ATM (3), BARD1 (1), BRCA2 (2), CHEK2 (1), PALB2 (2), RAD51C (1)	*HR alterations (n = 5 pts): ATM (1), CHEK2 (2), BARD1 (1), PALB2 (1)*
MMR alterations (n = 3 pts): MLH1 (3), MSH3 (1)	
RAF alterations (n = 6 pts): BRAF V600E (1), KANK4-RAF1 fusion (1), SND1-BRAF fusion (3), TBXAS1-BRAF rearrangement (1)	
NTRK alterations (n = 1 pt): ETV6-NTRK3 fusion (1)	

CONCLUSIONS

In our cohort, half of PACC patients presented with advanced disease. Unlike PDAC, PACC is a genomically diverse disease, with potentially targetable alterations in *RAF, HRD*, and *MMR* genes, offering additional therapeutic options for most of these patients. Therefore, somatic and germline testing should be considered for any patient diagnosed with PACC.

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