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Real World Outcomes with Chemotherapy and Immunotherapy in Metastatic Poorly Differentiated Gastroenteropancreatic Neuroendocrine Carcinomas

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BACKGROUND

Gastroenteropancreatic poorly differentiated neuroendocrine carcinomas (GEP-NECs) are aggressive cancers where cytotoxic chemotherapy (chemo) is the backbone of management. While the addition of immune checkpoint inhibitors (IOs) to chemo is recommended for lung NEC, evidence regarding IO efficacy in GEP-NECs is limited. We explore outcomes with systemic therapies in patients with metastatic GEP-NECs.

METHODS

Cases of metastatic GEP-NECs from 2018 and 2021 were identified within the USA's National Cancer Database (NCDB). Overall survival (OS) was analyzed using Kaplan-Meier estimations and Cox proportional hazards regression.

RESULTS

2,280 cases of metastatic GEP-NECs treated with chemo with survival data available were identified. Of these, 1748 (76.7%) received chemo alone, and 532 (23.3%) received chemo plus IO (ChemoIO). Patients treated with chemoIO had prolonged OS versus chemo alone (10.51 months [m] vs. 8.31 m; HR, 0.77; 95% CI, 0.69 – 0.85; p < 0.001). The association was significant in all histologies (small cell, p <0.001; large cell, p = 0.04; others, p = 0.01) and in some primary site subgroups (colorectal&anal, p <0.001; gastroesophageal, p = 0.02; others&unknown, p = 0.01; biliary, p = 0.78; pancreas, p = 0.48; small intestine, p = 0.73). The association was significant on multivariable analysis with select clinicopathological variables and comorbidity index (N = 2,235; Table).

Table: Multivariable Cox regression – select results

	HR (95% CI)	p-value
Chemo+IO (vs. Chemo alone)	0.71 (0.64 – 0.80)	<0.001
Age	1.004 (1.0003 – 1.008)	0.03

Primary (Ref: Colorectal&Anal)		
Gastroesophageal	0.86 (0.76 – 0.98)	0.02
Biliary	0.65 (0.53 – 0.80)	<0.001
Small Intestinal	0.65 (0.48 – 0.89)	<0.001
Pancreas	0.75 (0.66 – 0.85)	<0.001
Others (& Unknown)	1.00 (0.80 – 1.26)	0.97
Bone Mets (vs. Absent)	1.00 (0.80 – 1.26)	0.005
Liver Mets (vs. Absent)	1.37 (1.22 – 1.54)	<0.001
Lung Mets (vs. Absent)	1.24 (1.10 – 1.41)	<0.001
Primary Surgery (vs. No Surgery)	0.64 (0.55 – 0.73)	<0.001

CONCLUSIONS

Despite the limitations of the NCDB, combination chemoIO showed improved survival vs. chemo in metastatic GEP-NECs. Results of ongoing trials (NCT05058651) are awaited.

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