O-4

MEN1/DAXX alterations are associated with improved overall survival and treatment response in patients with pancreatic neuroendocrine tumors

Rushabh Gujarathi[1], Sara Abou Azar[2], Joseph Tobias[2], Xavier M. Keutgen[2], Chih-Yi Liao[1].

[1]Section of Hematology and Oncology, Department of Medicine, University of Chicago, Chicago, IL; [2]Section of Endocrine Surgery, Department of Surgery, University of Chicago, Chicago, IL.

BACKGROUND

Alterations in the *MEN1* and *DAXX* genes are common in pancreatic neuroendocrine tumors (PNETs). Previous data show that *MEN1*- and *DAXX*- altered tumors show longer overall survival (OS) and these alterations may increase radiation efficacy in tumor cells. We explored the associations of *MEN1* and *DAXX* alterations with clinical outcomes in PNETs.

METHODS

A retrospective chart review was conducted. Patients with PNETs seen at University of Chicago between 2013 and 2023 with available tumor NGS results were included. Patients with MEN1 syndrome were excluded. Cases with deleterious alterations (truncating mutations, missense mutations considered pathogenic, copy number losses) in the *MEN1* and *DAXX* genes were considered as *MEN1/DAXX* altered (*MEN1/DAXX*^{at}). The primary outcome was OS. The secondary outcome was progression free survival (PFS), after peptide receptor radionuclide therapy (PRRT), capecitabine/temozolomide (CAPTEM), and metastases debulking. Kaplan-Meier estimations and Cox proportional hazards regression analysis were conducted.

RESULTS

62 patients were included. Median follow-up was 42.1 months (IQR, 28 – 67.6). 28 (45.2%) patients were *MEN1/DAXX*^{at}. At diagnosis, the *MEN1/DAXX*wt (wild-type) and *MEN1/DAXX*^{at} groups had similar median age (55.5 years vs. 54.2 years; p = 0.99), presence of metastatic disease (26/34, 76.5%; vs. 22/28, 78.6% p = 0.99), extrahepatic metastases (12/34, 35.3%; vs. 11/28, 39.3% p = 0.8), or bone metastases (7/34, 20.6% vs. 2/28, 7.1%; p = 0.17). The MEN1/DAXXwt group showed a higher proportion of grade 3 disease (vs. grade 1/2; 12/34, 35.3% vs. 2/28, 7.1%; p = 0.01). OS after diagnosis (19 deaths recorded) was longer in the *MEN1/DAXX*^{at} group (median NR vs. 53.8 months; HR, 0.39; 95% CI, 0.15 – 1.03; log-rank p = 0.049). In patients with metastatic disease (N = 61), OS was longer after diagnosis of metastases in the *MEN1/DAXX*^{at} group (median NR vs. 53.5 months; HR, 0.33; 95% CI, 0.12 – 0.89; p = 0.03). PFS was longer with PRRT in the *MEN1/DAXX*^{at} group (N = 27; 26.5 months vs. 12.9 months; HR, 0.30; 95% CI, 0.12 – 0.77; p = 0.01). PFS did not vary significantly for CAPTEM treatment (N = 30; 17.8 months vs. 12.4 months; HR, 0.65; 95% CI, 0.28 – 1.53; p = 0.32) or metastases debulking (N = 38; 14.5 months vs. 11.3 months; HR, 0.77, 95% CI, 0.38 – 1.55; p = 0.46).

CONCLUSIONS

MEN1/DAXX altered PNETs may represent a subtype with favorable prognosis. *MEN1/DAXX*^{at} cases showed favorable response to PRRT. The clinical significance of these alterations in PNETs warrants further exploration.

ABSTRACT ID 28544