Abstract citation ID: bvac150.1010

Neuroendocrinology and Pituitary

ODP300

c-MET expression in MEN1-associated neuroendocrine tumors

Raisa Ghosh, MD, Maya Lee, BS, Rana Tora, BS, James Welch, MGC, CGC, Vaishali I. Parekh, BS, Jaydira del Rivero, MD, William F Simonds, MD, Lee Scott Weinstein, MD, Jenny E Blau, MD, Sunita K Agarwal, PhD, and Smita Jha, MD

Multiple studies have shown that approximately 50-70% of patients with MEN1 die of causes directly related to MEN1 particularly gastroenteropancreatic (GEP) neuroendocrine tumors (NETs). While non-functional GEP-NETs are the most common in the general population, gastrinomas (40%) are the most common functional GEP-NETs in patients with MEN1. c-MET is a proto-oncogene that encodes for c-MET, a tyrosine kinase receptor which promotes tumor cell motility, proliferation, survival, invasion, and metastasis. Studies in patients with sporadic gastrinomas and pancreatic NETs (PNETs) have shown that c-MET expression correlates with decreased survival.

While c-MET inhibitors are currently in various stages of investigation for treatment of carcinoids and sporadic PNETs, data regarding their efficacy in patients with MEN1-related GEP NETs is lacking. The majority of trials in patients with GEP-NETs exclude or do not report the number of patients with MEN1. Importantly, somatic MEN1 mutations are observed in 20-40% of sporadic NETs (gastrinomas, PNETs, lung NETs, etc.) but correlation of cMET expression with the presence of somatic or germline MEN1 mutations has not been reported. We sought to investigate the expression of c-MET in tumor tissue from germline MEN1 patients with metastatic GEP-

NETs. **Methods:** We identified subjects with a germline positive MEN1 mutation and pathologically confirmed distant metastasis who had a follow-up visit between 2018-2020. Of these, we selected subjects with available tissue specimens (including either multiple organ sources or different tumor types). Where available, we identified specimens from multiple source or tumor types. Immunohistochemistry (IHC) to detect c-MET was performed with anti-MET (Cell Signaling) using the DAKO IHC kit (Agilent). IHC slides were imaged and observed to score the level of c-MET staining (-, 1+ to 5+). A score of 3+ or higher was considered consistent with overexpression. We investigated if age at initial GEP-NET presentation, tumor type, tissue source, tumor grade, total number of surgeries for GEP-NET, number of sites of distant metastasis and disease status from overall GEP-NET burden over the preceding 12 months (stable/progressive) predicted c-MET expression. **Results:** Eight subjects with available tissue specimens were identified, of which six had tissue from multiple organs while five had tissue from multiple tumor types. Six subjects (75%) showed increased expression of c-MET in one or more tumor specimen(s). The frequency of c-MET overexpression varied with tumor types – carcinoids (n=2/2; 100%), gastrinomas (n=3/5; 60%) and nonfunctional tumors (n=3/6; 50%). c-MET expression also varied among different tumors in the same patient. Tumor tissue from liver (n=2/2), duodenum (n=3/4), stomach (n=1/1), ovary (n=1/1), pancreas (n= 1/5), and lymph nodes (n=1/3), all showed over-expression of c-MET. No clear predictors of c-MET overexpression emerged. **Conclusion:** Our finding suggests a role for c-MET expression in personalizing therapy for patients with MEN1-related NETs with distant metastases.

Presentation: Sunday, June 12, 2022 12:30 p.m. - 2:30 p.m., Sunday, June 12, 2022 12:48 p.m. - 12:53 p.m.