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Ki-67 Proliferative Index and the Tumor Grade Predict Progression Free Survival in Ileal Carcinoids

Deepti Dhall¹, Rugvedita Parakh¹, Richard Mertens¹, Girish Dhall², Catherine Bresee⁴, Delma Ines¹, Fai Chung¹, Marissa Li¹, Steven D Colquhoun³, Nicholas N Nissen³, Run Yu⁵, Hanlin Wang¹ and Edward Wolin⁶

¹Pathology, Cedars-Sinai Medical Center, Los Angeles, CA, United States

²Hematology and Oncology, Children's Hospital of Los Angeles, Los Angeles, CA, United States

³Liver Transplant Surgery, Cedars-Sinai Medical Center, Los Angeles, CA, United States

⁴Biostatistics, Cedars-Sinai Medical Center, Los Angeles, CA, United States

⁵Division of Endocrinology, Cedars-Sinai Medical Center, Los Angeles, CA, United States

⁶Medical Oncology, Samuel Oschin Comprehensive Cancer Institute, Los Angeles, CA, United States

Background: Ki-67 proliferative index (Ki-67) is suggested to be an important prognostic variable in neuroendocrine tumors and is included as one of the grading parameters in small bowel carcinoid tumors. The aim of this study is to determine the usefulness of Ki-67 and the corresponding tumor grade in predicting progression free survival in ileal carcinoids, especially in a metastatic setting.

Methods: Tumors from 60 patients with ileal carcinoids (well-differentiated neuroendocrine tumors) were studied. Ki-67 immunohistochemical stain was performed on the primary as well as selected metastatic tumor and quantitated by computer-assisted image analysis using Ariol™ system. The tumors were graded based on mitotic activity and Ki-67. Clinical and pathologic variables affecting the progression free survival were analyzed.

Results: There were 32 females and 28 males with a mean age of 58 years (range: 29-95 years). At the time of initial presentation, 9 (15%) patients had localized disease, 31 (52%) patients had regional (nodal/mesenteric) spread, and 20 (33%) patients had distant metastasis (stage IV). Fourteen out of 60 patients experienced disease progression. Patients with a higher initial stage were more likely to experience disease progression ($p = 0.005$), and a higher histologic grade was associated with a higher likelihood of disease progression ($p < 0.001$). Among the patients

presenting with stage IV disease at the time of initial diagnosis, Ki-67 was significantly greater in patients who experienced disease progression (mean Ki-67 of primary and metastatic tumors were 10% and 15%, respectively, in patients with progression versus 1% and 2%, respectively, in patients with no progression). The mean time to progression in patients with Ki-67 > 2% in the primary tumor was significantly less when compared with patients with Ki-67 ≤ 2% (30.9 ± 10.9 months versus 134.0 ± 9.7 months, p < 0.001)

Conclusion: Ki-67 predicts progression free survival in patients with ileal carcinoids.