C-55

Patterns of Care and Outcomes in Localized, Grade 3, Gastroenteropancreatic Neuroendocrine Neoplasms: A 10-Year Experience in a Tertiary Centre

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BACKGROUND: High-grade Gastroenteropancreatic Neuroendocrine Neoplasms (GEP-NEN) represent 5% of all GEP-NEN. Few high grade GEP-NEN present with localized disease, and therefore evidence is lacking on the best treatment approach for these patients.

METHODS: A retrospective analysis of patients diagnosed with a localized high-grade GEP-NEN (defined as having a Ki67 of > 20%) at Princess Margaret Cancer Centre between 2008 and 2017 was conducted. Kaplan-Meier and Cox proportional hazards methods were used to analyze progression free survival (PFS) and overall survival (OS) with treatment modality (surgery or chemotherapy ± other therapy), Ki67 and age as covariates in multivariate analysis.

RESULTS: Among 640 GEP-NENs treated during this timeframe, 32 (5%) presented with localized disease. The most common primaries were colon (31.3%) and pancreas (21.9%). Poorly differentiated tumours accounted for 15 (46.9%) patients, well-differentiated for 5 (15.6%), and either mixed/not reported for 12 (37.5%). The Ki67 was 21-60% in 34.4% patients and >60% in 62.5%. Surgery was the most frequent modality in 23 (71.8%) patients, followed by chemotherapy in 19 (59.4%) patients. Half of the patients were assigned to a multimodality treatment, of which surgery with chemotherapy was the most

common (N=10; 31.3%). Median OS was not reached, and median PFS was 22.2 months. The estimated 3-year OS and PFS rates were 69% (95% CI 55-88%), and 34% (95% CI 19-59%) respectively. In multivariate analysis, only surgery was associated with an improved PFS (HR 0.27 [95% CI 0.08-0.98]) with a HR of 0.29 [95% CI 0.05-1.45] for OS.

CONCLUSION: Surgery followed by chemotherapy were the most commonly used treatment modalities for localized, high grade GEP-NENs. Patients who had surgery had better PFS compared with those treated non-surgically, highlighting the importance of surgery in this patient population. Although the absolute number of patients is small, our experience represents some of the largest, contemporary cohorts examining localized high grade GEP-NENs.