

## **Prognostic Value of Chromogranin A and Alkaline Phosphatase in Patients with Advanced Neuroendocrine Tumor**

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**Background:** Serum chromogranin A (CgA) or alkaline phosphatase (AlkPhos) are routinely assessed in patients with advanced neuroendocrine tumor (NET) patients but their prognostic significance continues to be debated. We evaluated whether CgA or AlkPhos were associated with overall survival in a large, prospectively collected cohort of NET patients.

**Methods:** We identified patients with metastatic NET enrolled in an institutional database between 2003-10. CgA and AlkPhos levels, together with demographic features including age, gender, tumor histology, and tumor subtype were obtained and correlated with overall survival using the log-rank test. Hazard ratios for each serum biomarker were calculated using multivariate Cox regression, adjusting for these baseline characteristics. Each biomarker was modeled as a time-varying covariate to account for variability in time from initial metastatic diagnosis to time of biomarker test.

**Results:** We identified 526 patients who presented at our institution with metastatic NET. Of these, we obtained CgA values for 349 patients and obtained AlkPhos values for 350 patients. There were 146 and 153 deaths among those tested for CgA and AlkPhos, respectively. The median survival time from time of test (yrs, (95%CI)) for patients

with advanced NET and an elevated CgA was 4.95 (3.96, 5.47), as compared to 7.85 (6.14, -) for those at normal CgA limits ( $p < 0.0001$ ). The median survival time from time of test (yrs, (95%CI)) for patients with an elevated AlkPhos was 3.27 (2.48, 4.08), as compared to 7.13 (6.05, 9.37) for those at normal AlkPhos levels ( $p < 0.0001$ ). Using the adjusted time-varying model, either elevated CgA (aHR 3.97 (2.73, 5.75)  $p = 3.15E-13$ ) or elevated AlkPhos (aHR 2.4 (1.7, 3.4)  $p = 7.96E-07$ ) were adverse prognostic factors for patients with advanced NET.

**Conclusion:** In patients with advanced disease, elevated serum CgA or elevated AlkPhos are associated with shorter survival times, independent of other prognostic factors.