Comparative Study of Pulmonary and Extrapulmonary High Grade Neuroendocrine Carcinomas: A SEER Database Analysis of 210195 Cases

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Background: High-grade neuroendocrine carcinomas (NECs) are anatomically grouped into lung (L-NECs) or extra-pulmonary (EP-NECs) and histologically sub-typed into small-cell or large-cell NEC. EP-NECs are managed similar to L-NECs per current guidelines irrespective of site of origin or histological sub type. However, recent small studies show important clinical and epidemiological differences between these subgroups.

Methods: We performed an analysis of the Surveillance, Epidemiology, and End Results (SEER) program of NEC cases from 1973-2012 to describe the differences in NECs based on anatomic location, stage and histological sub-type.

Results: We identified 210195 cases (91.3% L-NECs; 8.7% EP-NECs). Based on relative proportions, we classified EP-NECs into gastroenteropancreatic (GEP-NECs, 34.4%), unknown primary (UP-NECs 32.6%) and other sites (Other-NECs 33%) with varying proportions of histological subtypes (small cell, large cell and other histologies)noted at each site. While L-NECs and UP-NECs increased in incidence from 1973 to 1988 before declining, GEP-NECs and other EP-NECs have increased. Stage at diagnosis varied according to primary tumor site with distant stage varying from 24% for Other-NECs to 40% for GEP-NECs. Survival varied significantly per stage with a substantial proportion of localized cases being alive at 5-year (range: 29% of L-NEC to 45% of Other-NECs) and according to histological sub-type with other histologies having best survival at most sites. Survival according to site ranged from 2.4 months for UP-NEC to 6.5 months for GEP-NECs. Primary site remained highly statistically significant for survival even after multivariate analysis with other prognostic variables ($p < 0.0001$).

Conclusion: We observed significant differences in incidence trends over time and large variations in outcomes depending on anatomical site and histological sub type. Our data do not support the current approach of grouping all NECs as one entity.

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