

P-8

Association of 5HIAA and Mortality in Neuroendocrine Tumor Patients: A Systematic Review and Meta-Analysis

Vijay N. Joish¹; Sandip Shah²; Helen Shao²; Chad McKee¹; Pablo Lapuerta¹; Jerome Zacks³

¹Lexicon Pharmaceuticals, Inc.; ²MKTXS; ³Icahn School of Medicine, Mt Sinai Health System

BACKGROUND: Excessive secretion of serotonin by the neuroendocrine tumor (NET) has been associated with tumor burden, fibrosis, and long-term complications of carcinoid heart disease. A systematic review and meta-analysis was conducted to estimate the association between 5-hydroxyindoaleacetic acid (5-HIAA), a marker of serotonin, and all-cause mortality in NET patients.

METHODS: A literature search was performed across PUBMED, EMBASE, and clinicaltrials.gov databases for NET studies between 2007-2017 that reported mortality and 24-hour urine 5-HIAA (mg/24h) results at baseline. Studies that reported more than one value, were averaged. Data from full-text articles meeting search criteria were extracted for analysis. Mortality was converted to rates per person-year (number of patients by months of study follow-up, divided by 12) and was log-transformed to normalize the data. A restricted maximum likelihood (REML) meta-regression model, which controls for study size and design, was used to estimate the relationship between 5HIAA and 1-year mortality.

RESULTS: Out of 1,710 potential publications, 12 studies reporting 5-HIAA (mean 147.2 mg/24h, range 4-358) and all-cause mortality (average 39%, range 13%-75% during each study period) met all search criteria and were included in the meta-analysis. These 12 studies represented 793 patients with a median

age of 60 years, 49% female, and a total of 3,788 person-years of follow-up. Across all studies, higher 5-HIAA levels were associated with higher mortality. Meta-regression showed that every increase of 10 mg/24h in 5-HIAA predicted an 12% (95%CI: 9.0% to 17.0%) increase in mortality rate ($p < 0.001$).

CONCLUSION: 5HIAA levels reported in the published literature for NET patients are multiples above the normal range of 9 mg/24h. Elevated 5-HIAA levels were predictive of all-cause mortality. Reducing 5-HIAA may lead to better long-term outcomes for NET patients.