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Chromogranin A as Surveillance biomarker in Patients with cARcinoids (CASPAR)

Qing Meng[1], Thorvardur R. Halfdanarson[2], Joshua Bornhorst[2], Henning Jann[3], Shagufta Shaheen[4], Run Zhang Shi[4], Daniel M. Halperin[1].

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Mayo Clinic, Rochester, MN; [3]Charité Universitätsmedizin Berlin, Berlin, Germany; [4]Stanford University Medical Center, Palo Alto, CA.

BACKGROUND

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) have highly heterogeneous growth rates, yielding broad ranges of radiographic imaging intervals in standard guidelines, creating uncertainty for clinicians and patients. Chromogranin A (CgA) is released by GEP-NET cells and has been associated with increased tumor burden. However, clinical utility of CgA measurement has been limited by the lack of prospective validation studies and by different sensitivity for radiographic progression according to NET tumor type and volume. The aim of this study was to evaluate prospectively the performance of the B·R·A·H·M·S CgA II KRYPTOR immunoassay to monitor disease progression in patients with grade 1/2 GEP-NETs . This is the first prospective validation of a pre-specified clinical algorithm for the interpretation of CgA values in patients with advanced GEP-NETs.

METHODS

This prospective, multi-center, observational study was designed to validate the performance of the B·R·A·H·M·S CgA II KRYPTOR assay in monitoring disease progression in a defined population of GEP-NET patients with minimal confounding from end organ dysfunction or concomitant medications (e.g. PPIs). Patients were followed for up to 36 months including the evaluation of tumor burden with RECIST 1.1 categorization by imaging (CT/MRI scans). A clinical cut-off for changes in CgA levels over time to indicate the risk that a tumor progression occurred was derived from an observational pilot study. An increase of at least 50% in CgA concentration to an absolute value of >100ng/ml was considered positive.

RESULTS

175 adult patients were enrolled, and 153 patients had measurable disease at baseline and ≥1 follow-up visit. Using the cut-off for CgA increase resulted in a sensitivity of 34.4% (95%-CI: 25.6% - 44.3%, $p < 0.001$) and a specificity of 93.4% (95%-CI: 90.4% – 95.5%, $p < 0.001$) for radiographic progression. Positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) to diagnose whether a tumor progression occurred according RECIST 1.1 criteria were 57.9% (95% CI: 45.0-69.8), 84.3% (95% CI: 80.5-87.6), 5.20 (95% CI: 3.23-8.36), and 0.70 (95% CI: 0.61-0.81), respectively. The AUC was estimated at 0.731 (95% CI: 0.670-0.793).

CONCLUSIONS

B·R·A·H·M·S™ CgA II KRYPTOR™ can be used as an aid in monitoring disease progression for patients with grade 1/2 gastroentero-pancreatic neuroendocrine tumors, with NPV as its greatest strength.