Neuroendocrine Tumor Blood Transcript Analysis, the NETest, Predicts Gastroenteropancreatic Neuroendocrine Tumor Disease Status and is Prognostic for Progressive Disease

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Principal Message

NETest correlates with clinical disease status and levels (>70%) are prognostic for well-differentiated GEP-NET progression (per REGIST).

NETest <40% correlated with disease stability over ~5-years identifying this molecular signature also is predictive.

Patients clinically categorized as stable with high NETest levels (>70%) develop disease progression in 100% of cases within 2 years.

Background

A key issue in GEP-NETs is early identification and prediction of disease progression. Clinical evaluation and imaging are limited due to the lack of sensitivity and disease indolence. We assessed the utility of the NETest as a predictive and prognostic marker of progression in a long-term follow-up study.

Methods

GEP-NETs (n=31) followed for a median 4 yrs (2.2-5.4). WHO tumor grade/stage Grade I: n=15, Grade II: n=16; 31 (91%): stage IV. Baseline and longitudinal imaging and biomarkers were available and progression defined (RECIST 1.0). NETest: qPCR and multi-analyte algorithmic analysis (disease activity scaled 0-100% with low <40% and high activity risk cutoffs >80%); CgA: RIA (normal <150µg/l); PFS: Kaplan-Meier analysis. A quantitative disease activity score was also developed (cumulative sum of disease activities (s) across all preceding time points) and affinity propagation algorithms used to cluster longitudinal patient disease activity profiles.

Results

At baseline, 100% were NETest-positive and CgA was elevated in 50%. Baseline NETest (>80%) was significantly associated (p=0.01) with disease progression (median PFS 0.68 yrs vs. 2.78 yrs with <40% levels). NETest was more informative (96%) than CgA changes (Δ+25%) in consistently predicting disease alterations (40%, p=2×10^{-5}, Chi^{2}=18). The NETest had an earlier time-point change than imaging (1.02±0.15 yrs). Baseline NETest levels >40% in stable disease were 100% prognostic of disease progression vs CgA (Chi^{2}=5.0, p<0.03). Baseline NETest values <40% accurately (100%) predicted stability over 5-ys (p=0.05, Chi^{2}=3.8 vs. CgA).

Conclusion

NETest correlated with well-differentiated GEP-NET clinical status. It identified clinically-actionable alterations ~1 year before image-based evidence of disease progression.