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NETest2.0® Accurately Detects Active Disease and Monitors Recurrence in Neuroendocrine Tumors: Results from the RegisterNET Registry

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BACKGROUND

Reliable biomarkers for disease detection and longitudinal surveillance of neuroendocrine tumors (NETs) remain an unmet clinical need. NETest2.0® is a blood-based, machine-learning–enhanced multigene transcript assay developed to assess NET disease activity. We evaluated its ability to detect disease and monitor recurrence or progression in a large prospective registry cohort.

METHODS

RegisterNET (NCT02270567) is a multicenter observational registry of NET patients. Two analyses were performed. First, NETest2.0® results were compared with contemporaneous imaging findings in 1,290 samples from 886 patients. Second, longitudinal changes in NETest2.0® scores were evaluated in 404 patients with paired samples obtained a median of 7 months apart. Clinical cohorts included post-operative minimal residual disease assessment, recurrence surveillance following curative-intent surgery, watch-and-wait monitoring, and treatment response assessment. Imaging (CT, MRI, or SSTR-PET) served as the clinical comparator.

RESULTS

For disease detection, NETest2.0® demonstrated an AUC of 0.96 with 91.9% sensitivity, 94.9% specificity, 98.4% positive predictive value, and 92.5% overall accuracy. Performance was maintained across tumor grades, primary sites, and imaging modalities.

Among 404 patients undergoing longitudinal surveillance, 286 remained stable or disease-free and 118 experienced recurrence or progression. NETest2.0® scores decreased in stable/responding patients (median −14.6%) but increased in patients with recurrence/progressive disease (median +15.4%; $p<0.0001$). Changes in NETest2.0® scores

yielded an AUC of 0.86 for identifying progression. Using a positive NETest2.0® result with any increase in score, specificity reached 98.3%, positive predictive value 91.1%, and overall accuracy 83.9%.

CONCLUSIONS

NETest2.0® accurately identifies active NET disease and provides clinically meaningful longitudinal surveillance information across diverse management settings. Serial molecular assessment distinguished stable from progressive disease and demonstrated high specificity for recurrence/progression. These findings support incorporation of NETest2.0® into risk-adapted surveillance strategies to complement imaging and potentially reduce unnecessary radiologic monitoring.

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