The NETest™ score was developed for well-differentiated, low grade (WHO Grade I and II) gastroenteropancreatic NETs. It is scaled from 0 (lowest risk) to 100% (highest risk). Scores are linked to event free survival (image-defined disease progression). In general, lower scores are associated with lower risks of disease recurrence, longer event free survival and a longer time to disease progression. High scores are linked to shorter event free survival and a shorter time to disease progression. Gastrointestinal tract NETs e.g., small bowel, have better outcomes than pancreatic NETs, Grade I have better outcomes than Grade II.

A high risk score (≥80%) is associated with poor outcome irrespective of grade or site.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Date.Reported</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>NETest</td>
<td>40%</td>
<td>4/20/2017</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

Comments: Value (40) falls into the low range. Interpretation: Scores although low have begun to increase (last result = 27; 2/25/2016).

Laboratory Director Signature: ________________________________
NETest™ Methodology and Score Calculation

The NETest™ score is an algorithm assessment of 51 normalized neuroendocrine tumor transcripts resulting from PCR amplification in peripheral blood (EDTA-collected) samples [1-3]. The algorithm was derived from mathematical models and multivariate analysis of PCR data and has been tested in 2000 patient samples [1-9]. It has high sensitivity (>95%) and specificity (>95%) for gastroenteropancreatic NETs [2-5]. GEP-NETs (WHO Grade I and II) are the target group. The algorithm and scaling has not been specifically developed for other tumor grades or types, although the NETest may be positive and elevated, e.g., in MEN-1 or other neuroendocrine-related neoplasia e.g., paraganglioma or pheochromocytoma [10]. No specific interpretations or clinical recommendations, however, can be made in these cases.

Laboratory Developed Test (LDT)

This test was developed and its performance characteristics determined by Wren Laboratories LLC, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) and is qualified to perform high-complexity clinical laboratory testing. This LDT has not been approved by the US Food and Drug Administration (FDA) but the FDA has determined that such clearance is not necessary. This test should be used for clinical purposes in combination with patient history, condition, symptoms, etc. under the guidance of the patient's provider. The results cannot be interpreted as absolute evidence for the presence or absence of malignant disease. Medication: The test is unaffected by PPIs but NETest scores can be reduced by somatostatin analogs [4, 6]. Interventions: Peptide Radioreceptor Therapy (PRRT), embolization (bland or chemical), radiofrequency ablation and surgery, have been noted in the short-term (during intervention and up to 3 months), to increase circulating levels in some cases [7, 8].

Clinical Implications of the NETest™ Score

Overview

Low NETest, irrespective of tumor burden, grade and treatment is associated with a longer PFS [6, 9].

High NETest, irrespective of tumor burden, grade and treatment is associated with a shorter PFS [6, 9].

Surgery

Low NETest, in the absence of image-detectable disease, suggests no or minimal disease [7].

High NETest, in the absence of image-detectable disease, suggests residual disease and is associated with disease recurrence, particularly for NETest scores 65-100% [7].

Standard Treatment Protocols

Low NETest, irrespective of tumor burden or grade is associated with a longer PFS [9]. This is considered useful for monitoring tumor efficacy.

High NETest, irrespective of tumor burden or grade is associated with a shorter PFS [9]. This is considered useful for identifying a decrease in treatment efficacy or an indication of tumor progression.

Monitoring Protocols

Consecutive low NETest scores correlate with tumor stability and identify low progression or a response to therapy [6, 9]. Increases in consecutive NETest scores to values 80-100% correlate with tumor growth and predict image-confirmation of tumor progression [6, 9].

References