WREN Laboratories | NETest®

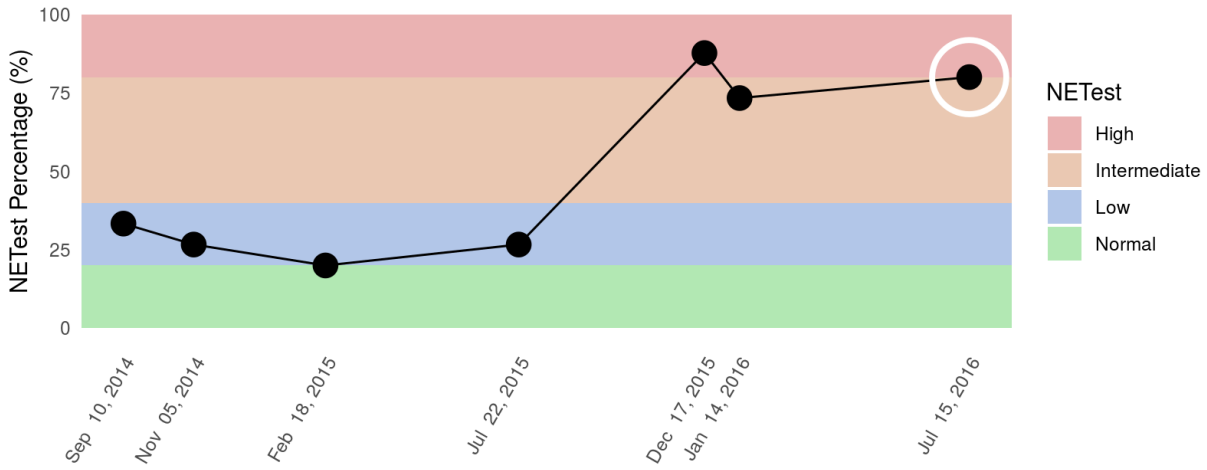
Patient Information	
NAME:	XXXXX XXXXX
DOB:	XX/XX/XXXX
PHONE:	(XXX)XXX-XXXX
PDx #:	0010000032
ICD 10:	XXXXX

Sample Information	
SAMPLE NUMBER:	10001203
BLOOD COLLECTED:	15 Jul. 2019
DATE RECEIVED:	15 Jul. 2019
DATE REPORTED:	19 Jul. 2019
TEST:	NETest™

Provider Information	
REFERRING PHYSICIAN:	XXXXX XXXXX, MD
NPI:	XXXXXXXXXXX
PRACTICE:	XXXXXXXXXXX

NETest™ Results

Test	Result	Date.Reported	Remark
NETest	80%	7/19/2016	High



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 ($\geq$80%) is associated with poor outcome irrespective of grade or site.

Comments: *NETest levels are high and fall into the progressive or active disease category. Recommendation: Discuss treatment plan with NET specialist.*

Mark Kidd PhD

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 collected samples [1-3]. The algorithm was derived from mathematical models and multivariate analysis of PCR data and the gene signature has been tested and independtly validated [4-8]. It has high sensitivity (>95%) and specificity (>95%) for gastroenteropancreatic and bronchopulmonary NETs (grade I-II; typical and atypical carinoids) [5-18]. 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., Grade II NETs or neuroendocrine carinomas (NEC) [11], in MEN-1 or other neuroendocrine-related neoplasia e.g., paraganglioma or pheochromocytoma [13]. No specific interpretations or clinical recommendations, other than the identification of tumors with a neuroendocrine phenotype, 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. The assay has been validated pursuant to CLIA regulations and is used for clinical purposes. It has not been cleared or approved by the FDA but the FDA has determined that such clearance is not necessary.
Medication: The test is unaffected by PPIs but NETest scores can be reduced by somatostatin analogs [5, 12, 16].
Interventions: Peptide Radioreceptor Therapy (PRRT), embolization (bland or chemical), radiofrequency ablation and surgery, have been noted in the short-term (during intervention), to increase circulating levels in some cases [14, 15]. Decreased scores after completion of therapy is associated with treatment efficacy [5, 9-12, 14, 15].

Clinical Implications of the NETest™ Score

Overview

Low NETest ($\leq$ 40), is associated with a longer PFS [5, 9-16].
High NETest ($\geq$ 40), is associated with a shorter PFS [5, 9-16].

Surgery

Low NETest (0-40), in the absence of image-detectable disease, suggests no or minimal disease [5, 9-11, 15].
High NETest (41-100) indicates residual disease. A high NETest, in the absence of image-detectable disease, indicates active recurrent disease [5, 9-11, 15].

Standard Treatment & Monitoring Protocols

Low NETest ($\leq$ 40), is considered useful for demonstrating treatment efficacy [5, 6, 9-14, 16]. Consecutive low NETest scores correlate with tumor stability and identify slow progression or a response to therapy [5, 6, 9-16].
High NETest ($\geq$ 40), is considered useful for identifying tumor progression despite treatment [5, 6, 9-14, 16]. Increases in consecutive NETest scores <40 correlate with tumor growth and predict image-confirmation of tumor progression [5, 6, 9-16].

References

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