Executive Summary: The Afirma® Gene Expression Classifier

The Afirma® Gene Expression Classifier (Veracyte, Inc.; South San Francisco, CA) is a 142 gene expression assay that produces a benign or suspicious result when analyzing thyroid nodule fine needle aspirate (FNA) biopsy specimens that are cytologically indeterminate (i.e. not clearly benign or malignant under the microscope). Physicians order Afirma GEC testing pre-operatively to identify benign nodules and avoid unnecessary thyroid surgery. When patients with thyroid nodules are screened for thyroid cancer with FNA biopsy, 15%-30% are diagnosed indeterminate. Since indeterminate nodules have a 25% risk of malignancy, these patients are routinely referred for diagnostic thyroid surgery even though 75% are found to be benign post-operatively. The Afirma GEC test improves patient health outcomes by pre-operatively reclassifying cytologically indeterminate thyroid nodules as benign, avoiding unnecessary surgery.

The published medical evidence supporting the Afirma GEC assay is robust, including two prospective multicenter, double-blind clinical validity studies, and 18 studies of clinical utility. Since thyroid FNAs with indeterminate cytology are routinely referred to surgery, the key performance goal of the Afirma GEC test is Negative Predictive Value (NPV), i.e. the accuracy of a benign test result. A landmark study published in the New England Journal of Medicine demonstrated Afirma GEC’s ability to reclassify indeterminate nodules as benign with an NPV of 95% (i.e. a risk of cancer of 5% or less). This low 5% risk of cancer is comparable to the risk of cancer to patients with a benign cytology diagnosis. Thyroid cancer guideline experts regard this low risk of cancer as sufficient to replace surgery with observation.

Eighteen published clinical utility studies, including three long-term clinical outcome studies and two cost effectiveness and quality of life studies, reporting on the management of 2,085 patients across 52 academic medical centers and community practices have shown that nearly one-half of patients tested result as Afirma GEC benign, resulting in a number needed to test (NNT) of approximately 2 patients to avoid 1 diagnostic surgery. Among Afirma GEC benign patients, 90% were managed through watchful waiting in lieu of diagnostic thyroid surgery. In three recently published long-term outcome studies of patients with Afirma GEC benign results, 86% of patients avoided unnecessary thyroid surgery during median follow up times of 13 to 26 months. Collectively, these three studies demonstrate the durability of the Afirma benign result and support the decision of physicians and patients who elect to avoid thyroid surgery for low risk nodules. When clinical decision making is guided by an Afirma benign result, long-term surgery rates are low and patient outcomes are improved.

Several published clinical practice guidelines and specialty society statements support the use of Afirma GEC. The National Comprehensive Cancer Network (NCCN) Thyroid Carcinoma Guidelines v1.2016 recommend physicians consider molecular diagnostic testing, including Afirma GEC, in lieu of immediate surgical resection to identify patients with indeterminate thyroid nodules at a low risk of cancer that may be observed clinically. The 2015 American Thyroid Association thyroid cancer guidelines recommend molecular testing to assess risk of malignancy in lieu of proceeding to immediate diagnostic surgery for cytologically indeterminate nodules. In addition, a statement by the American Thyroid Association (ATA) Surgical Affairs Committee recommends that Afirma GEC benign patients may be managed with active surveillance.

Afirma is a well-validated, pre-operative diagnostic test that is recommended by national guidelines to help avoid unnecessary diagnostic thyroid surgeries. Multicenter follow-up studies show that patients managed with Afirma GEC undergo fewer diagnostic thyroid surgeries. This level of evidence has made Afirma GEC the standard of care for management of indeterminate thyroid nodules, improving treatment decision making for physicians and their patients.


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