



PATIENT INFORMATION

PATIENT: John Doe		DOB: 01 Jan 1973	GENDER: M	LAB ID: L123	MRN: M123
COLLECTION DATE	24 Sep 2019	FACILITY NAME	University Hospital of Anytown		
RECEIVED DATE	26 Sep 2019	SUBMITTING PHYSICIAN	Jane Demo	PHONE (555) 555-5555	
REPORT DATE	26 Sep 2019	TREATING PHYSICIAN/CC	---	PHONE ---	
CLINICAL HISTORY: History of Cancer: Family History of Thyroid Cancer: No, History of I(131) radiation or external radiation therapy: No, Suspicious Ultrasound Characteristics: Nodule A: Hypoechoic, Solid: >95% solid					

RESULTS

Nodule: **A** 1.45 cm, Lower Right

AFIRMA GENOMIC SEQUENCING CLASSIFIER	AFIRMA XPRESSION ATLAS			
<p>Suspicious (Risk of Malignancy ~50%)</p> <p>MTC: Negative Parathyroid: Negative</p>	<p>BRAF:p:K601E c.1801A>G</p> <p>BRAF:p:V600E c. 1799T>A: Negative RET/PTC1, RET/PTC3: Not Detected</p>			
	Clinical Relevance	Risk of Malignancy	Associated Neoplasm Type	FDA Approved Therapy [#]
	Potential clinical significance in thyroid cancer	~50% ¹¹	Follicular neoplasms (FA, NIFTP, FVPTC, FTC)	No alteration-specific therapy currently approved

RESULTS INTERPRETATION

The result of this 1.45cm nodule A is Afirma GSC Suspicious and **BRAF:p:K601E c.1801A>G** positive which suggests a risk of cancer of ~50%.¹¹ This genomic alteration is associated with follicular neoplasms (FA, NIFTP, FVPTC, FTC) and a RAS-like profile, which includes rates of lymph node metastases and extrathyroidal extension that are lower than BRAF V600E-like neoplasms, but higher than Non-BRAF-Non-RAS-like neoplasms.^{9,10} Clinical correlation and surgical resection should be considered.

GROSS DESCRIPTION

Received one vial of FNAProtect, labeled with the Requisition Form # and patient initials.

E-SIGNED ON 26 Sep 2019 12:51 PM BY:

Robert J Monroe MD, PhD, Veracyte Inc. CLIA # 05D2014120
6000 Shoreline Ct, Suite 100, South San Francisco, CA 94080
Test Methodology: RNA Sequencing

CLIA#05D2014120, #45D2052137
CA License CLF340176, COS00800859
Lab Director: Robert J Monroe, MD, PhD

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TEST PERFORMANCE

Afirma GSC ^{1,5}	Cytopathology Diagnosis Indeterminate*	MTC ^{3,5}	BRAF ^{1,2,5,11}	RET/PTC ^{2,5,7,11}	Parathyroid ^{5,6}
Risk of Malignancy: Afirma GSC Benign	~4%	>99% / >99%	>99% / >99%	>99% / >99%	>99% / >99%
Risk of Malignancy: Afirma GSC Suspicious	~50%				
Sensitivity:	91%				
Specificity:	68%				
Limit of Detection†:	5%				
		Sensitivity/Specificity			
		PPA/NPA			
		Confirmation Rate/NPA			
		Risk of Malignancy			
		Limit of Detection†			

	BRAF V600E ^{1,4,5}	Afirm Xpression Atlas ^{7,8} (Afirm GSC suspicious, suspicious for malignancy, or malignant cytopathology)	
		Nucleotide Variant Panel**	Fusion Panel***
NPA	>99%	>99%	>99%
PPA	>99%	74%	82%
Confirmation Rate [§]	>98%	>98%	>99%
Limit of Detection [¶]	5%	5%	10%

References: 1. Patel KN, et al. *JAMA Surg* 2018. 2. Haugen BR, et al. *Thyroid* 2016. 3. Randolph G, et al. *ATA* 2017. 4. Angell TE, et al. *ATA* 2017. 5. Hao, et al. *Frontiers in Endo* 2019. 6. Sosa JA, et al. *ATA* 2017. 7. Angell, et al. *Frontiers in Endo* 2019. 8. Data on file. 9. TCGA Research Network. *Cell* 2014 10. Yoo, et al. *PLoS Genetics* 2016 11. Goldner, et al. *Thyroid* 2019. 12. Stack, et al. *ATA* 2019.

* Indeterminate includes Atypia of Undetermined Significance / Follicular Lesion of Undetermined Significance and (suspicious for) Follicular Neoplasm / Hürthle Cell Neoplasm.
 † Analytical sensitivity studies demonstrated the test's ability to detect malignant cells in a background of benign cells.
 ‡ BRAF classifier performance is based on a comparison to a castPCR DNA assay for the BRAF V600E mutation.
 ** Nucleotide variant performance, excluding BRAF V600E, is based on a comparison to a DNA AmpliSeq assay that measures variants using a 5% variant allele frequency threshold.
 *** Fusion performance is based on a comparison to an RNA AmpliSeq fusion assay and TaqMan assays.
 § Confirmation rate is the proportion of positive calls that are confirmed positive by the reference method.
 ¶ Analytical sensitivity studies demonstrate the test's ability to detect a positive variant in a background of wild type.
 # FDA approved therapies for thyroid cancer, both specific for genomic alterations and non-specific, may be found at <https://www.cancer.gov/about-cancer/treatment/drugs/thyroid> and <https://www.cancer.gov/about-cancer/treatment/drugs/solid-tumors>. See <https://clinicaltrials.gov> for potentially relevant clinical trials. Afirma XA is not a companion diagnostic and is not conclusive for any therapy.

Associated Neoplasm Type abbreviations – FA, Follicular Adenoma; FTC, Follicular Thyroid Carcinoma; FVPTC, Follicular Variant of Papillary Thyroid Carcinoma; NIFTP, Noninvasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features; PTC, Papillary Thyroid Carcinoma.

This NGS assay cannot differentiate somatic and germline variants. Further testing and/or genetic counseling may be warranted depending on the patient's clinical findings, family history and/or variant identified.

Afirma Thyroid FNA Analysis is a diagnostic service provided by Veracyte, Inc. for the assessment of thyroid nodules that includes cytopathology and gene expression testing. Afirma GSC, BRAF, MTC and RET/PTC tests and their performance characteristics were determined by Veracyte. MTC is an RNA classifier that identifies the presence of medullary thyroid carcinoma (MTC); BRAF is a BRAF p. V600E, c. 1799T>A RNA classifier; RET/PTC is a gene expression marker of somatic rearrangements of the RET protooncogene (RET/PTC1 and RET/PTC3).

Afirma Xpression Atlas (XA) is a diagnostic service provided by Veracyte, Inc. Afirma XA sequences 511 genes to measure the presence or absence of 761 nucleotide variants and 130 fusion pairs. The performance characteristics were determined by Veracyte. Genomic coordinates or full list of genes and variants available upon request.