Afirma
THYROID FNA ANALYSIS

VV20008

REPORT STATUS: Final
PAGES: 1 of 2
CLIENT ID: 97
AFIRMA REQ: R123

PATIENT REPORT

Sample Patient Report

PATIENT INFORMATION

PATIENT: John Doe | **DOB:** 01 Jan 1973 | **GENDER:** M | **LAB ID:** L123 | **MRN:** M123

COLLECTION DATE	18 Sep 2019	**FACILITY NAME**	University Hospital of Anytown		
RECEIVED DATE	20 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

CYTOPATHOLOGY

I	II	III	IV	V	VI
Non Diagnostic	Benign	**Atypia of Undetermined Significance**	Suspicious for Follicular Neoplasm	Suspicious for Malignancy	Malignant

Cytopathology Diagnosis: Indeterminate - Atypia of Undetermined Significance

Diagnostic Comments: These features are best categorized as atypia of undetermined signficance.

Microscopic Description: The cytologic and cell block preparations are sparsely cellular and contain only microfollicles and scant colloid.

AFIRMA GENOMIC SEQUENCING CLASSIFIER

Suspicious (Risk of Malignancy ~50%)

MTC: Negative
Parathyroid: Negative

AFIRMA XPRESSION ATLAS

***BRAF*:p:K601E c.1801A>G**

***BRAF*:p:V600E c. 1799T>A:** Negative
***RET/PTC1, RET/PTC3*:** Not Detected

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 Bethesda III 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 CytoLyt and one vial of FNAprotect, each 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

CYTOPATHOLOGY E-SIGNED ON 20 Sep 2019 11:22 AM BY:
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Lab Director: Robert J Monroe, MD, PhD

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TEST PERFORMANCE

Afirma GSC[1,5]	**Cytopathology Diagnosis Indeterminate***
Risk of Malignancy: **Afirma GSC Benign**	~4%
Risk of Malignancy: **Afirma GSC Suspicious**	~50%
Sensitivity:	91%
Specificity:	68%
Limit of Detection†:	5%

	MTC[3,5]	***BRAF***‡,[2,5,11]	***RET/PTC***[2,5,7,11]	**Parathyroid**[5,6]
Sensitivity/Specificity	>99% / >99%			>99% / >99%
PPA/NPA		>99% / >99%		
Confirmation Rate/NPA			>99% / >99%	
Risk of Malignancy	>99%	>95%	>95%	
Limit of Detection†	20%	5%	10%	15%

	BRAF V600E‡,[4,5]	**Afirma Xpression Atlas**[7,8] (Afirma 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.

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