Afirma®

Thyroid FNA Analysis

VZ42062

REPORT STATUS: Final
PAGES: 1 of 2
CLIENT ID: 96
AFIRMA REQ: radreport70

PATIENT REPORT

Patient Sample Report

PATIENT INFORMATION

PATIENT: John Doe | **DOB:** 19 Jul 1976 | **SEX:** M | **LAB ID:** | **MRN:**

COLLECTION DATE	27 Jan 2023	**FACILITY NAME**	Production Test Clinic - DemoData		
RECEIVED DATE	28 Jan 2023	**SUBMITTING PHYSICIAN**	Jane Doe	**PHONE**	---
REPORT DATE	06 Mar 2023	**TREATING PHYSICIAN/CC**	---	**PHONE**	---

CLINICAL HISTORY: Suspicious Ultrasound Characteristics: Nodule A: Microcalcifications

RESULTS

Nodule: A Thyroid, Upper Left, 1.2 cm

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 (AUS - Bethesda Category III)

Diagnostic Comments: These features are best classified as atypia of undetermined significance.

Microscopic Description: The cytologic and cell block preparations are sparsely cellular and show a few clusters of follicular cells in crowded or microfollicular groups and some colloid.

AFIRMA GENOMIC SEQUENCING CLASSIFIER

Ensemble Classifier	Xpression Atlas	Other Classifiers	
Benign (Risk of Malignancy ~4%)	**N/A**	***BRAF* p. V600E c. 1799T>A:** Negative ***RET*/*PTC1*, *RET*/*PTC3*:** Not Detected	**MTC:** Negative **Parathyroid:** Negative

TERT PROMOTER REGION

***TERT* c.-124C>T (C228T):** Test Not Performed (TNP)
***TERT* c.-146C>T (C250T):** Test Not Performed (TNP)

NODULE A RESULTS SUMMARY

The result of this 1.2cm Bethesda III nodule A is Afirma GSC Benign, which suggests a low risk of cancer at approximately 4%. Treatment like a cytologically benign nodule may be appropriate, including clinical correlation. Afirma XA is not performed on GSC Benign nodules[7]. *TERT* promoter region analysis is not performed on GSC Benign nodules.

GROSS DESCRIPTION

A: Received 1 vial(s) of sample(s) in CytoLyt, 1 vial(s) of FNAprotect

CYTOPATHOLOGY REVIEWED AND E-SIGNED ON 28 Jan 2023 07:21 PM BY:
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TEST PERFORMANCE

Afirma GSC - Ensemble Classifier [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* V600E** [1,2,4,5,11]	***RET*/*PTC*** [2,5,7,11]	**Parathyroid** [5,6]	**XA Nucleotide Variant Panel****	**XA Fusion Panel*****	**TERT** [8]
Sensitivity	>99%			>99%			
Specificity	>99%			>99%			
PPA		>99%			74%	82%	>99%
NPA		>99%	>99%		>99%	>99%	>99%
Confirmation Rate			>99%		>98%	>99%	>99%
Limit of Detection	20%	5%	10%	15%	5%	10%	5%

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. **13.** Whitmer D, et al. *Frontiers in Endo* 2022.

* 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 molecular testing. The Ensemble Classifier, Parathyroid Classifier, MTC Classifier, *BRAF* V600E Classifier, XA, DNA assay of the *TERT* promoter region, and their performance characteristics were determined by Veracyte. The Ensemble Classifier measures the expression profile of RNA isolated from the nodule and classifies the sample as benign or suspicious for malignancy. The Parathyroid Classifier determines if the FNA specimen is positive or negative for parathyroid tissue. The Medullary Thyroid Carcinoma (MTC) Classifier determines if the nodule is positive or negative for MTC. The *BRAF* V600E Classifier measures RNA isolated from the nodule and classifies the sample as positive or negative for the *BRAF* V600E mutation. The *RET*/*PTC* assay sequences the *RET* and *PTC* genes to detect *RET*/*PTC1* and *RET*/*PTC3* fusions and reports them as detected or not detected. XA evaluates 593 genes included in Afirma GSC for 905 specific variants and 235 specific fusion pairs. The DNA analysis evaluates the two *TERT* promoter variants, C228T and C250T.

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