Afirma®

Genomic Sequencing Classifier

VZ42303

REPORT STATUS: Final
PAGES: 1 of 2
CLIENT ID: 96
AFIRMA REQ: BZ233011

PATIENT REPORT

Patient Sample Report

PATIENT INFORMATION

PATIENT: John Doe | **DOB:** 12 Oct 1970 | **SEX:** F | **LAB ID:** L123 | **MRN:** M123

COLLECTION DATE	27 Feb 2023	**FACILITY NAME**	Production Test Clinic - DemoData		
RECEIVED DATE	01 Mar 2023	**SUBMITTING PHYSICIAN**	Jane Doe	**PHONE**	---
REPORT DATE	06 Mar 2023	**TREATING PHYSICIAN/CC**	---	**PHONE**	---

CLINICAL HISTORY: No clinical history provided on the Afirma test requisition form

RESULTS

Nodule: A Thyroid, Lower Right, 1.45 cm

AFIRMA GENOMIC SEQUENCING CLASSIFIER

Ensemble Classifier

Suspicious

Xpression Atlas

BRAF:p.K601E c.1801A>G

Other Classifiers

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

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

TERT PROMOTER REGION

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

NODULE A RESULTS SUMMARY

The result of this 1.45cm Bethesda III nodule A is Afirma GSC Suspicious and *BRAF* p.K601E 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. Consider visiting clinicaltrials.gov to see if there are any available clinical trials relevant to the described molecular variant/fusion discovered on Afirma testing.

GROSS DESCRIPTION
A: Received 1 vial(s) of FNAprotect

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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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