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AUTHORIZED DISTRIBUTOR

natera™ | Signatera™ Residual disease test (MRD)

Signatera Residual Disease Test (MRD)

Patient Details

Patient Name:

Date of Birth: Sex:

Natera Case File ID:

Accession ID:

Sample ID – FFPE Tumour:

Sample ID – Peripheral Blood:

Date Sample Received – FFPE Tumour:

Date Sample Received – Peripheral Blood:

Date of Report:

Test Ordered:

Ordering Physician

Name:

Address:

No. Street

City Province Postal Code

Fax:

Copy To

Name:

Fax:

The specimen you submitted recently for Signatera MRD testing was referred by LifeLabs Genetics to Natera Inc for analysis. Attached please find the laboratory test report issued by Natera. If you have any questions or concerns regarding this result, please contact LifeLabs Genetics at 1-84-GENEHELP (1-844-363-4357) or Ask.Genetics@lifelabs.com.

Authorized by:

R.F. Carter, PhD, FCCMG
Laboratory Director
LifeLabs Genetics

LifeLabs Genetics is accredited by Accreditation Canada and the College of American Pathologists (CAP) and is licensed by the Ontario Ministry of Health and Long-Term Care to operate as a clinical genetic laboratory: MOHLTC license 5806.

cap ACCREDITED

IQMH ISO 15189 *Plus*™ Accredited Medical Laboratory

natera™

Certified Lab

LifeLabs GENETICS®

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ABOUT THIS TEST:

Signatera™ is a bespoke mPCR-NGS assay for detection of circulating tumor DNA (ctDNA) in the plasma of patients previously diagnosed with cancer. Individual-specific mutation signatures are identified by up front tissue and matched normal whole exome sequencing.

Patient & Sample Information

Patient Name:	[redacted]
Date of Birth:	
Medical Record #:	N/A
Case File ID:	[redacted]
Cancer Type:	
Tissue Collected:	
Tissue Received:	
Plasma Collected:	
Plasma Received:	
Date of Surgery:	
Block ID:	
Block Type:	Block

Ordering Physician

Name:	[redacted]
Clinic:	LifeLabs LP
NPI:	N/A
Address:	100 International Blvd., Toronto, Ontario M9W 6J6, CA
Pathology Lab Name:	LifeLabs LP
Additional Reports:	N/A
Report Date:	02/28/2023

FINAL RESULTS SUMMARY

Signatera Negative

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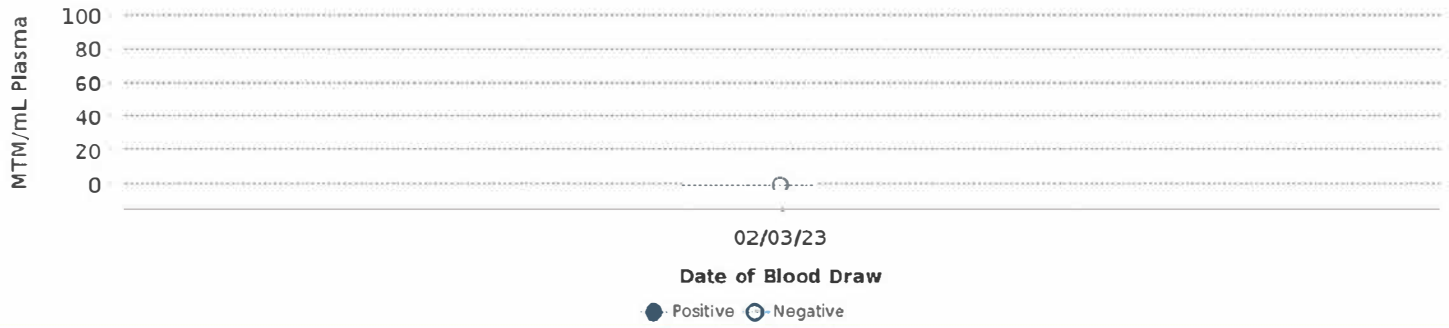
MTM/mL:
Not Detected

Mean tumor molecules per mL is calculated based on the mean of ctDNA molecules detected per mL of the patient's plasma. ***See Limitations section below.***

Historical Results



Date	Reported MTM/mL
Feb 03, 2023	0.00

Interpretation and Limitations

Signatera is a personalized, tumor-informed test for the longitudinal detection of circulating tumor DNA (ctDNA). Interval testing is recommended for all patients. Studies have demonstrated that when ctDNA is detected (Signatera Positive) following surgery or definitive treatment, the risk for disease relapse is high without further treatment. Conversely, when ctDNA is not detected, the patient may be considered at lower risk for relapse. For those with multiple timepoints, upward trending ctDNA levels are suggestive of increasing tumor burden (1,2). For a single time point in isolation, the absolute MTM/mL value has no known clinical significance and should not be compared across patients. Test results should be interpreted in context of other clinicopathological features. ctDNA detection sensitivity may be limited due to blood collection within two weeks of surgery and while the patient is on therapy. Signatera is a quantitative test and reports in units of mean tumor molecules per ml (MTM/ml.), which is comprised of three measured components (plasma volume, cell free DNA (cfDNA) concentration, and Variant Allele Frequency (VAF)). The MTM/mL number will be qualified if any measured component falls outside the analytical measurement range for that component. The analytical sensitivity is 95% at the limit of detection (0.3 MTM/mL). Results obtained are specific to the assessed time point. A negative test result does not definitively indicate the absence of cancer. This test is not designed to detect or report germline variation, nor does it infer hereditary cancer risk for the patient. Each Signatera assay is designed to a single tumor for a given patient. At this time, multiple personalized Signatera assays cannot be developed for the same patient. This test is designed to detect ctDNA from the assayed tumor only; new primary tumors will not be detected. There is a low risk that a new primary may share a variant that could interfere with the Signatera test. Testing cannot be performed in patients who are pregnant, have a history of bone marrow transplant, or history of blood transfusion within three months. This test is expected to have limited sensitivity in cancer types such as GIST, renal cell carcinomas, primary brain tumors, and lymphoma due to limited ctDNA shed.

[1] Bratman SV, Yang SYC, Iafolla MAJ, et al. Personalized circulating tumor DNA analysis as a predictive biomarker in solid tumor patients treated with pembrolizumab. Nature Cancer. 2020;1(9):873-881

[2] Henriksen TV, Tarazona N, et al., Circulating Tumor DNA in Stage III Colorectal Cancer, beyond Minimal Residual Disease Detection, toward Assessment of Adjuvant Therapy Efficacy and Clinical Behavior of Recurrences. Clin Cancer Res. 2021; 28(3):507-517

Methodology

FFPE samples are assessed by a pathologist to identify tumor margins and percent tumor content. Tumor DNA is extracted using Qiagen AllPrep. Whole genomic DNA is isolated from peripheral blood using QIAamp DNA Blood Mini Kit to provide a baseline DNA sequence. Circulating tumor DNA (ctDNA) is extracted from plasma derived from whole blood samples collected in cell-free DNA blood tubes (Streck) using the QIAsymphony automated or manual extraction method (Qiagen). Whole-exome sequencing is performed on tumor and peripheral blood DNA using KAPA HyperPrep library kit (Roche) with a custom xGen exome capture (IDT). Using a proprietary algorithm, putative clonal variants present in the tumor but absent in the germline DNA are identified to design the customized multiplex PCR assay. The customized PCR assays are run to detect presence or absence of these variants within circulating plasma. A patient's plasma sample is considered ctDNA positive when at least two individual-specific tumor variants are detected. When fewer than two individual-specific tumor variants are observed, a negative result is issued. Tumor variation outside of the individual, tumor specific variants is not assessed. Pathology services and whole exome sequencing are performed at Ashion Analytics (CLIA ID# 03D2048606) 445 N. Fifth Street, Phoenix, AZ 85004.

Disclaimer

The extraction, library preparation, and sequencing for this test were performed by Natera Inc., 201 Industrial Rd. Suite 410, San Carlos, CA 94070 (CLIA ID 05D1082992). The data analysis and reporting for this test were performed by Natera Inc., 201 Industrial Rd. Suite 410, San Carlos, CA 94070 (CLIA ID 05D1082992). This test was developed and its performance characteristics determined by Natera Inc. The test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). CAP accredited, ISO 13485 certified, and CLIA certified. Pathology services and whole exome sequencing for this test were performed by Ashion Inc, 445 N 5th St., Phoenix AZ 85004, CLIA # 03D20486.

Approved by: J. Dianne Keen-Kim, Ph.D., FACMGG, Senior Laboratory Director