

**Patient & Sample Information**

Patient Name:  
 Date of Birth:  
 Medical Record #:  
 Case File ID:  
 Cancer Type: TNBC  
 Tissue Collected: 01/29/2016  
 Tissue Received: 01/31/2016  
 Plasma Collected: 09/17/2017  
 Plasma Received: 09/19/2017

**Ordering Physician**

Name:  
 Clinic:  
 NPI:  
 Address:  
 Additional Reports:  
 Report Date:

**ABOUT THIS TEST:**

Signatera™ is an individual-specific 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 upfront tissue and matched-normal whole exome sequencing.

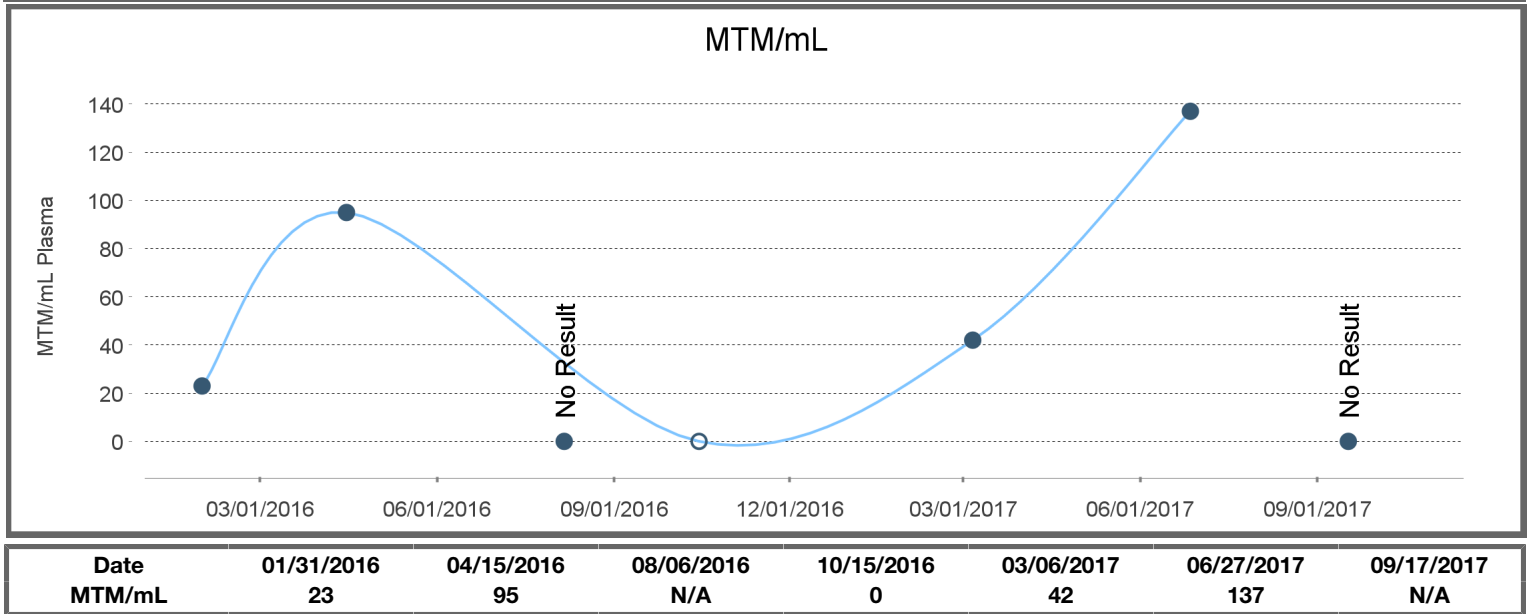
**FINAL RESULTS SUMMARY****Signatera: No result**

**Mean Tumor Molecules/mL**  
**Not Determined**

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

Laboratory processing of this specimen could not yield results. Submission of a repeat specimen is not recommended.

Test Clinical Notes

**Historical Results**

**Patient & Sample Information**

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Date of Birth:  
Medical Record #:  
Case File ID:  
Cancer Type: TNBC  
Tissue Collected: 01/29/2016  
Tissue Received: 01/31/2016  
Plasma Collected: 09/17/2017  
Plasma Received: 09/19/2017

**Ordering Physician**

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Address:  
  
Additional  
Reports:  
Report Date:

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**Interpretation and Limitation**

This test has been validated for use in patients with colorectal, bladder, lung and breast cancer. The test cannot be run on patients with concurrent malignancies, who are pregnant, who have a history of bone marrow transplant, history of blood transfusion within three months. Signatera is a screening test, is not diagnostic, and does not infer therapeutic choice. All results should be interpreted by a clinician.

**Methodology**

FFPE samples are assessed by a pathologist to identify tumor margins and percent tumor content. 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 is extracted from plasma collected in Streck tubes using Natera's proprietary methods. Whole-exome sequencing using KAPA HyperPrep library kit (Roche) with a custom xGen exome capture (IDT) is performed to identify tumor DNA sequence using a proprietary algorithm. Sixteen putative clonal variants present in the tumor but absent in the baseline DNA form the basis for individual-specific PCR-based assays. Individual-specific PCR assays are run to detect presence or absence of circulating tumor DNA (ctDNA). 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. Results obtained are specific to the assessed time point. A positive test result does not indicate a clinical diagnosis of cancer. A negative test result does not indicate remission. This test is not designed to detect or report germline variation, nor infer hereditary cancer risk for the patient. Tumor variation outside of the sixteen individual-specific tumor variants are not assessed. Pathology services and whole exome sequencing were performed at Ashion Analytics, Phoenix, AZ and reported on 04/01/2017

**Disclaimer**

This test was developed and its performance characteristics determined by Natera, Inc. (CLIA ID #05D1082992) as required by the CLIA '88 regulations. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA), but due to enforcement discretion by the FDA, FDA clearance or approval is not necessary at this time.

**Approved by:**

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

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**Patient & Sample Information**

Patient Name:  
Date of Birth:  
Medical Record #:  
Case File ID:  
Cancer Type: Colon cancer  
Tissue Collected: 05/18/2020  
Tissue Received: 05/29/2020  
Plasma Collected: 07/09/2020  
Plasma Received: 07/13/2020  
Date of Surgery:  
Block ID:  
Block Type:

**Ordering Physician**

Name:  
Clinic:  
  
NPI:  
Address:  
  
Pathology  
Lab Name:  
Test Order:  
Additional  
Reports:  
Report Date: 07/22/2020

**FINAL RESULTS SUMMARY**

**Signatera Negative**

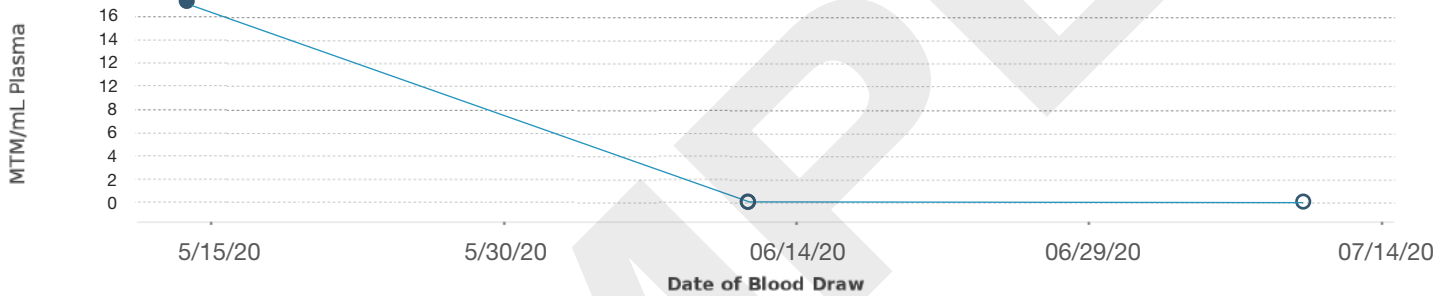


**MTM/mL:  
Not Detected**

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

Test Clinical Notes

**Historical Results**



Date	MTM/mL
May 14, 2020	16.96
Jun 12, 2020	0.00
Jul 09, 2020	0.00

**Interpretation, Recommended Test Intervals, 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. Test results should be interpreted within clinical context. ctDNA detection sensitivity may be limited due to blood collection within two weeks of surgery and while the patient is on therapy. The analytical sensitivity of Signatera is > 95% at 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. 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.

**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. 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. Circulating tumor DNA is extracted from plasma collected in Streck tubes using Natera's proprietary methods. 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**

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

**Approved by:** Eric Crawford, PhD, FACMGG, Laboratory Director

**ABOUT THIS TEST:**

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**Patient & Sample Information**

Patient Name:  
Date of Birth:  
Medical Record #:  
Case File ID:  
Cancer Type: Colon cancer  
Tissue Collected: 03/30/2018  
Tissue Received: 07/19/2019  
Plasma Collected: 07/08/2020  
Plasma Received: 07/09/2020  
Date of Surgery:  
Block ID:  
Block Type:

**Ordering Physician**

Name:  
Clinic:  
  
NPI:  
Address:  
  
Pathology  
Lab Name:  
Test Order:  
Additional Reports:  
Report Date: 07/16/2020

**FINAL RESULTS SUMMARY**

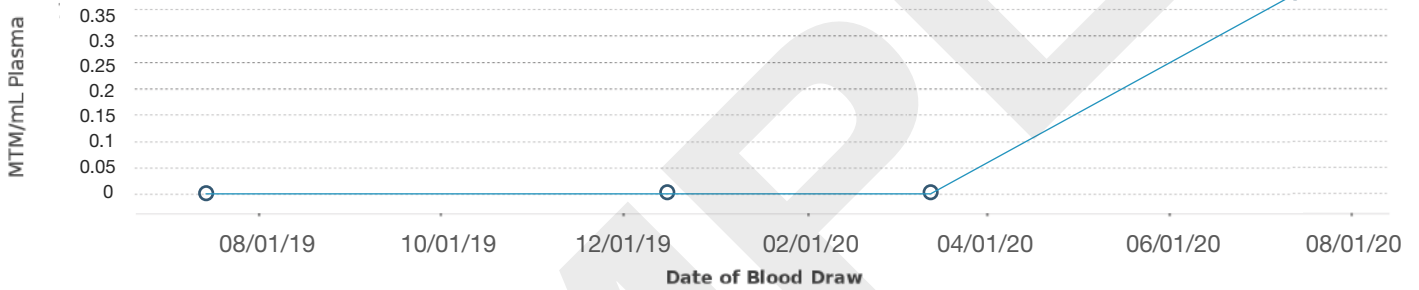
**Signatera Positive**



Date: 07/08/2020  
MTM/mL: 0.38

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

**Historical Results**



Date	MTM/mL
Jul 09, 2019	0.00
Dec 16, 2019	0.00
Mar 12, 2020	0.00
Jul 08, 2020	0.38

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**Patient & Sample Information**

Patient Name:  
Date of Birth:  
Medical Record #:  
Case File ID:  
Cancer Type: Colon cancer  
Tissue Collected: 05/18/2020  
Tissue Received: 05/29/2020  
Plasma Collected: 07/09/2020  
Plasma Received: 07/13/2020  
Date of Surgery:  
Block ID:  
Block Type:

**Ordering Physician**

Name:  
Clinic:  
NPI:  
Address:  
Pathology  
Lab Name:  
Test Order:  
Additional Reports:  
Report Date: 07/22/2020

**FINAL RESULTS SUMMARY**

**Signatera Negative**

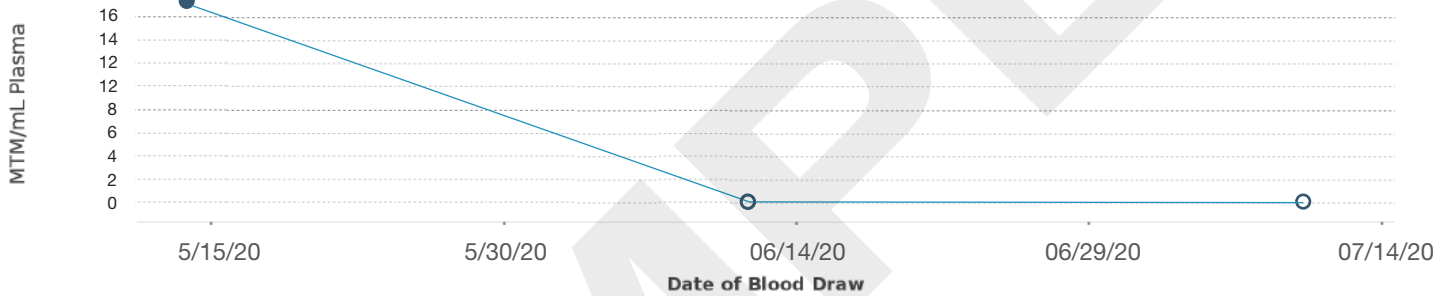


**MTM/mL:  
Not Detected**

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

Test Clinical Notes

**Historical Results**



Date	MTM/mL
May 14, 2020	16.96
Jun 12, 2020	0.00
Jul 09, 2020	0.00

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Patient Name:  
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Medical Record #:  
Case File ID:  
Cancer Type: Colon cancer  
Tissue Collected: 03/30/2018  
Tissue Received: 07/19/2019  
Plasma Collected: 07/08/2020  
Plasma Received: 07/09/2020  
Date of Surgery:  
Block ID:  
Block Type:

**Ordering Physician**

Name:  
Clinic:  
  
NPI:  
Address:  
  
Pathology  
Lab Name:  
Test Order:  
Additional  
Reports:  
Report Date: 07/16/2020

**FINAL RESULTS SUMMARY**

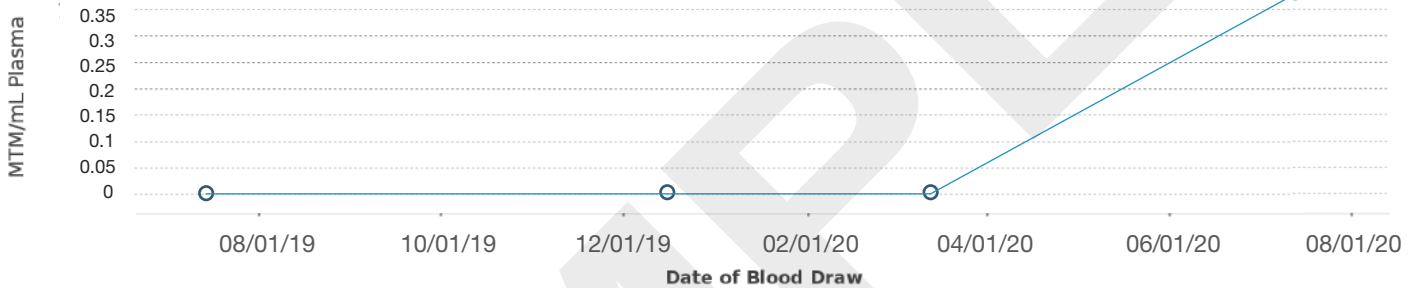
**Signatera Positive**



Date: 07/08/2020  
MTM/mL: 0.38

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**Historical Results**



Date	MTM/mL
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Dec 16, 2019	0.00
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