BioReference LABORATORIES
an OPKO Health Company

Final Report

PHYSICIAN
ACCOUNT, INACTIVE
BIOREFERENCE/COPY T.PINON
481B EDWARD ROSS DRIVE
SUITE 100
ELMWOOD PARK, NJ 07407
ACCT #: **J3333** **XY9**
P:(201) 421-2004 F:(201) 421-2004

PATIENT
TEST, TEST
DOB: 01/01/1951 **Age:** 68Y **Sex:** M
Surgical #: S-111
Patient ID: P-111
Address: 123 MAIN STREET
NEW CITY, NY 10956

SAMPLE
Specimen ID: **304371407**
Date Reported: 08/26/2019 3:02 PM
Date Collected: 06/12/2019 7:00 AM
Date Received: 08/22/2019 1:33 PM
Source: Lung, right
Clinical Information: NSCLC, WIDELY METASTATIC

OnkoSight Next Generation Sequencing Tumor Mutation Burden

RESULTS

TUMOR MUTATION BURDEN: HIGH

Mutations/Megabase: 27.66

COMMENT

Presence of >=10 mutations / megabase has been reported to be therapeutically predictive of favorable clinical outcomes and responsiveness to immune checkpoint inhibitors, according to some studies (N Engl J Med 2018; 378:2093-2104). Consensus standardization for this biomarker remains an ongoing imperative (Genes Chromosomes Cancer. 2019 Jan 21). MSI status evaluation may also be of interest, if clinically indicated.

METHODOLOGY

Histologic review is performed by an appropriately board certified pathologist to guide tissue microdissection and DNA isolation from tumor enriched areas. Specimens with minimal tumor cellularity may be rejected. Multiplex PCR for targeted next-generation sequencing using semi-conductor-based detection of pH change is performed. The sequenced sample is a PCR-amplified fragment library in which each sample is uniquely identified by ligation of a short oligonucleotide barcode. The assay detects single base substitutions and short insertion/deletions in the exons of 409 oncogenes, targeting a total of 1.65 million bases. Tumor Mutation Burden is reported as number of nonsynonymous mutations in one (1) megabase of genomic coding sequence. Each sample is monitored for quality to ensure reliable mutation detection. Variants are bioinformatically identified by an automated process that takes into account statistical confidence of base calling and alignment and mapping quality [Ion Reporter software version 5.10.3.0 or higher]. The software requires a minimum number of 400 reads to detect a mutation. Likely germline mutations are bioinformatically filtered and excluded.

Reportable Range: For full list of interrogated genes please refer to:https://www.genpathdiagnostics.com/oncology/ngs-personalized-medicine/

REFERENCES

1. Stenzinger et al (2019) Genes Chromosomes Cancer. Jan 21.
2. Buttner et al (2019) ESMO Open. Jan 24; 4(1).
3. Hellman et al (2018) New England Journal of Medicine 378 (22): 2093-2104
4. Ready, K et al (2019). Journal of Clinical Oncology 37 (12): 992-1000
5. Rizvi et al. (2015). Science 348 (6230): 124-128
6. Journal for Immunotherapy for Cancer 2018, 6 (Suppl 2):O48

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Pathologist, ex. 7567
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Laboratory Director

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PATIENT
TEST, TEST
DOB: 01/01/1951 **Age:** 68Y **Sex:** M
Surgical #: S-111
Patient ID: P-111
Address: 123 MAIN STREET
NEW CITY, NY 10956

SAMPLE
Specimen ID: **304371410**
Date Reported: 08/26/2019 3:11 PM
Date Collected: 06/12/2019 7:00 AM
Date Received: 08/22/2019 1:33 PM
Source: Lung, right
Clinical Information: NSCLC, WIDELY METASTATIC

OnkoSight Next Generation Sequencing Tumor Mutation Burden

RESULTS

TUMOR MUTATION BURDEN: LOW

Mutations/Megabase: 8.0

COMMENT

Presence of fewer than 10 mutations / megabase has been associated with lower rates of response to targeted immunotherapeutic agents, according to some studies (N Engl J Med 2018; 378:2093-2104). Consensus standardization for this biomarker remains an ongoing imperative (Genes Chromosomes Cancer. 2019 Jan 21). MSI status evaluation may also be of interest, if clinically indicated.

METHODOLOGY

Histologic review is performed by an appropriately board certified pathologist to guide tissue microdissection and DNA isolation from tumor enriched areas. Specimens with minimal tumor cellularity may be rejected. Multiplex PCR for targeted next-generation sequencing using semi-conductor-based detection of pH change is performed. The sequenced sample is a PCR-amplified fragment library in which each sample is uniquely identified by ligation of a short oligonucleotide barcode. The assay detects single base substitutions and short insertion/deletions in the exons of 409 oncogenes, targeting a total of 1.65 million bases. Tumor Mutation Burden is reported as number of nonsynonymous mutations in one (1) megabase of genomic coding sequence. Each sample is monitored for quality to ensure reliable mutation detection. Variants are bioinformatically identified by an automated process that takes into account statistical confidence of base calling and alignment and mapping quality [Ion Reporter software version 5.10.3.0 or higher]. The software requires a minimum number of 400 reads to detect a mutation. Likely germline mutations are bioinformatically filtered and excluded.

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PATIENT
TEST, TEST
DOB: 01/01/1951 **Age:** 68Y **Sex:** M
Surgical #: S-111
Patient ID: P-111
Address: 123 MAIN STREET
NEW CITY, NY 10956

SAMPLE
Specimen ID: **304371409**
Date Reported: 08/26/2019 3:08 PM
Date Collected: 06/12/2019 7:00 AM
Date Received: 08/22/2019 1:33 PM
Source: Lung, right
Clinical Information: NSCLC, WIDELY METASTATIC

OnkoSight Next Generation Sequencing Tumor Mutation Burden

RESULTS

TUMOR MUTATION BURDEN: CANCELLED

METHODOLOGY

Histologic review is performed by an appropriately board certified pathologist to guide tissue microdissection and DNA isolation from tumor enriched areas. Specimens with minimal tumor cellularity may be rejected. Multiplex PCR for targeted next-generation sequencing using semi-conductor-based detection of pH change is performed. The sequenced sample is a PCR-amplified fragment library in which each sample is uniquely identified by ligation of a short oligonucleotide barcode. The assay detects single base substitutions and short insertion/deletions in the exons of 409 oncogenes, targeting a total of 1.65 million bases. Tumor Mutation Burden is reported as number of nonsynonymous mutations in one (1) megabase of genomic coding sequence. Each sample is monitored for quality to ensure reliable mutation detection. Variants are bioinformatically identified by an automated process that takes into account statistical confidence of base calling and alignment and mapping quality [Ion Reporter software version 5.10.3.0 or higher]. The software requires a minimum number of 400 reads to detect a mutation. Likely germline mutations are bioinformatically filtered and excluded.

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PATIENT
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DOB: 01/01/1951 **Age:** 68Y **Sex:** M
Surgical #: S-111
Patient ID: P-111
Address: 123 MAIN STREET
NEW CITY, NY 10956

SAMPLE
Specimen ID: **304371408**
Date Reported: 08/26/2019 3:04 PM
Date Collected: 06/12/2019 7:00 AM
Date Received: 08/22/2019 1:33 PM
Source: Lung, base of left
Clinical Information: NSCLC, WIDELY METASTATIC

OnkoSight Next Generation Sequencing Tumor Mutation Burden

RESULTS

TUMOR MUTATION BURDEN: QUANTITY NOT SUFFICIENT

COMMENT

The specimen submitted for testing did not contain sufficient tumor material, therefore testing was cancelled. Too little tumor material results in inadequate amounts of nucleic acid to successfully perform the assay. If additional material is available and submitted, sample re-analysis can be performed.

METHODOLOGY

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