ContextualGenomics

Sonic Genetics
Quality is in our DNA

Melanie Citizen

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Referring Doctor	Dr John Medico
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Address	123 Main Street, SUBURBTOWN NSW 2000
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Requested	17 May 2018
Collected	18 May 2018 09:00 am
Received	18 May 2018 12:27 pm
Reported	25 May 2018 15:46 pm

Contextual Genomics Report
FIND IT® NSCLC Panel (EGFR,ERBB2,BRAF,KRAS,MET)

Summary

- Activating EGFR variant detected.
- Treatment with EGFR tyrosine kinase inhibitors (TKIs) may be considered.
- No EGFR TKI resistance variants have been detected.

MUTATIONS DETECTED*

Gene	cDNA change	Amino Acid Change	Exon	Allelic ratio (%)	Therapeutic implication	Level of evidence
EGFR	c.2573T>G (NM_005228.3)	L858R p.(Leu858Arg)	21	63.3	Indication for treatment with erlotinib, gefitinib, afatinib	Tier: I.A NCCN PBS

* No mutations were detected in the ERBB2, MET, BRAF, KRAS genes. All hotspot mutations detected in this specimen are shown in the Mutations Detected table, above. All tested mutations are listed in the "Hotspot Panel" table (below, after Methodology). Mutations listed in the "Hotspot Panel" but not presented above were tested, but were not detected in this specimen.

Interpretation

An activating EGFR variant has been **DETECTED** in the tumour DNA of this patient. The presence of such a variant is a PBS criterion for treatment of NSCLC with EGFR TKIs such as gefitinib, erlotinib and afatinib.

NO variants conferring resistance to first- or second-generation EGFR TKIs (including EGFR T790M and exon 20 insertions) have been detected.

Clinical trials

Australia	Study
EGFR Mutation Present	
A Phase I/II, Open-Label, Multicentre Study to Investigate the Safety, Tolerability, Pharmacokinetics and Anti-tumour Activity of AZD4205 as Monotherapy or in Combination With Osimertinib in Patients With EGFR Mutant Advanced Stage Non-Small Cell Lung Cancer (NSCLC)	NCT03450330
Other Relevant Trials	
A Phase II Study of Navarixin (MK-7123) in Combination With Pembrolizumab (MK-3475) in Participants With Selected Advanced/Metastatic Solid Tumors	NCT03473925
A Phase Ib/II, Open-Label, Multicenter, Randomized Umbrella Study Evaluating The Efficacy And Safety Of Multiple Immunotherapy-Based Treatment Combinations In Patients With Metastatic Non-Small Cell Lung Cancer (Morpheus-Lung)	NCT03337698

The clinical trials included in the report are sourced from Australian trials listed on clinicaltrials.gov and anzctr.org.au. We select trials based on tumour histotype and mutation status, with a specific focus on trials of targeted therapy. The inclusion of a trial in our report does not necessarily mean that the patient would be eligible. Patients' eligibility for a trial, and the benefit that they may derive from it, will depend on additional factors that must be assessed by the oncologist. Conversely, the list of potentially relevant trials in our report may not be complete. We may have overlooked relevant trials on these websites, or there may be relevant trials listed elsewhere. Please let us know if you identify a trial of targeted therapy that could have been included in a patient's report.

Specimen Information

Specimen Type: FFPE Block

Specimen Source: Biopsy

Primary Site of Tumour: Lung

Histologic Type: Adenocarcinoma

Referral Reason : Therapeutic Target ID

Biopsy Site : Lung

Block ID #: BLOCK #12345

Tumour Cellularity: 15%

Methodology and Limitations

This test involves targeted sequence analysis of hotspot mutations/coding exons of the requested genes and transcripts (listed below, see Hotspot Panel table). DNA is extracted and targets of interest amplified using a highly multiplexed in-house designed PCR assay, sequenced using Illumina technology and analysed using a validated, custom-built bioinformatics pipeline. Hotspot variants are categorised into clinical significance tiers as per Li et al. 2017 (PMID 27993330). Variants of strong or potential clinical significance (tier I or II) will be reported. VUS and likely benign variants (tier III and IV) will not be reported. Please contact the laboratory if tier III or IV variants are required.

Single nucleotide changes, insertions (1-18 bp) and deletions (1-24 bp) are detected by this assay. Limit of detection is approximately 5% variant allele ratio; the ability to detect a particular mutation may depend upon the tumour content of the tested sample and the proportion of the mutant tumour clone. Rare genetic variation can interfere with this assay. CNVs (e.g. gene amplification or large

deletions) and gene rearrangement events (e.g. gene fusions) will not be detected by this assay. Approximately 20% of MET exon 14 skipping mutations are large deletions, and will not be detected. BRCA gene mutations, MSI and tumour mutational burden are not assessed in this assay. This assay does not differentiate between germline (hereditary) and somatic mutations.

Hotspot Panel					
Gene	**Hotspot**	**Transcript**	**Gene**	**Hotspot**	**Transcript**
BRAF	Q201, G466, F468, G469, Y472, D594, G596, L597, V600, K601	NM_004333.4	KRAS	G12, G13, A59, Q61, K117, A146	NM_004985.4
EGFR	S492, exons: 18, 19, 20, 21	NM_005228.3	MET	Y1253, exons: 13, 14+25, 14-50, 14, 18	NM_001127500.2
ERBB2	G309, S310, L755, exons: 20	NM_004448.3			