CANCER GENETICS®

Empowering Personalized Cancer Treatment

LUNG COMPLETE

Lung Complete™

Almost 225,000 new cases of lung cancer are diagnosed each year. It is estimated that 41% of lung cancer tumors are driven by certain genetic mutations that could be targets for specific drugs. Non-small cell lung cancer (NSCLC) accounts for about 85% of all lung cancers. Multiple lung cancer testing guidelines including the NCCN guidelines, detail targeted therapies associated with genetic alterations of specific biomarkers.

Empowering Personalized Medicine

Clinicians have long known that patients respond differently to treatment. Genomics is now helping them in apprehending each patient's unique genetic make-up and the probable outcome of their disease. Testing patients for specific biomarkers can provide insight into diagnosis, prognosis, and the patient's likelihood of responding to certain treatments.

Tests being offered in the Complete™ Programs include biomarkers that rely on various methodologies and that have diagnostic and prognostic significance for each patient.

Lung Biomarkers

Genetic Alteration	Frequency	Clinical Utility
EGFR mutations	10-35%	Sensitizing mutations benefit from erlotinib, gefitinib & afatinib targeted therapies.
ALK rearrangements *c-MET* expression *ROS1* rearrangements	3-7% 2-4% 1%	Genetic alterations benefit from crizotinib targeted therapy.
PD-L1 expression	24%	Target for PD1/PD-L1 immunotherapy.
KRAS mutations	15-25%	Prognostic of poor survival independent of therapy & predicts lack of benefit from *EGFR* TKIs.

List of Lung Complete™ Tests

Physicians can order tests individually or allow CGI pathologists and directors to devise a panel evaluation as determined necessary.

Morphology & IHC

Morphology

Morphological and histologic subtype assessments provide diagnostic information for lung cancer.

IHC Evaluation

This panel provides diagnostic information on the immunophenotype of lung cancer. Panel includes antibodies to confirm carcinoma of lung primary and to subclassify lung cancer (CK 7, TTF-1, Napsin A, p63, CK 5/6) as well as c-MET and PD-L1 antibodies. Overexpression of MET is associated with poor prognosis and acquired resistance to *EGFR* tyrosine kinase inhibitor (TKI) treatments.

Molecular Diagnostics

EGFR Mutation Analysis

EGFR mutations predict sensitivity or resistance to *EGFR* TKI treatments such as erlotinib and gefitinib. The most common *EGFR* mutations that show higher rates of response to *EGFR* TKIs, include the deletion of exon 19 and the L858R point mutation in exon 21. The predicted response rate to erlotinib is ~82-83% and to gefitinib is ~71-73% for these *EGFR* TKI sensitive mutations. The T790M point mutation in exon 20 is the most common mechanism of acquired resistance to *EGFR* TKIs.

KRAS Mutation Analysis

The *KRAS* mutation predicts resistance to *EGFR* TKIs and is associated with a poor overall survival independent of therapy.

FISH

ALK Break Apart DNA-FISH Probe

The *ALK* Break Apart DNA-FISH probe identifies rearrangements of the *ALK* gene which indicated resistance to *EGFR* TKI therapy. Patients with *ALK* gene rearrangements can benefit from *ALK* TKIs such as crizotinib. The predicted response rate to crizotinib is >60%.

ROS1 DNA-FISH Probe

ROS1 gene rearrangements are similar to *ALK* gene rearrangements. Similarly, patients with *ROS1* gene rearrangements can benefit from *ALK* TKIs. The predicted response rate to crizotinib in patients with *ROS1* gene rearrangements is 57.1%.

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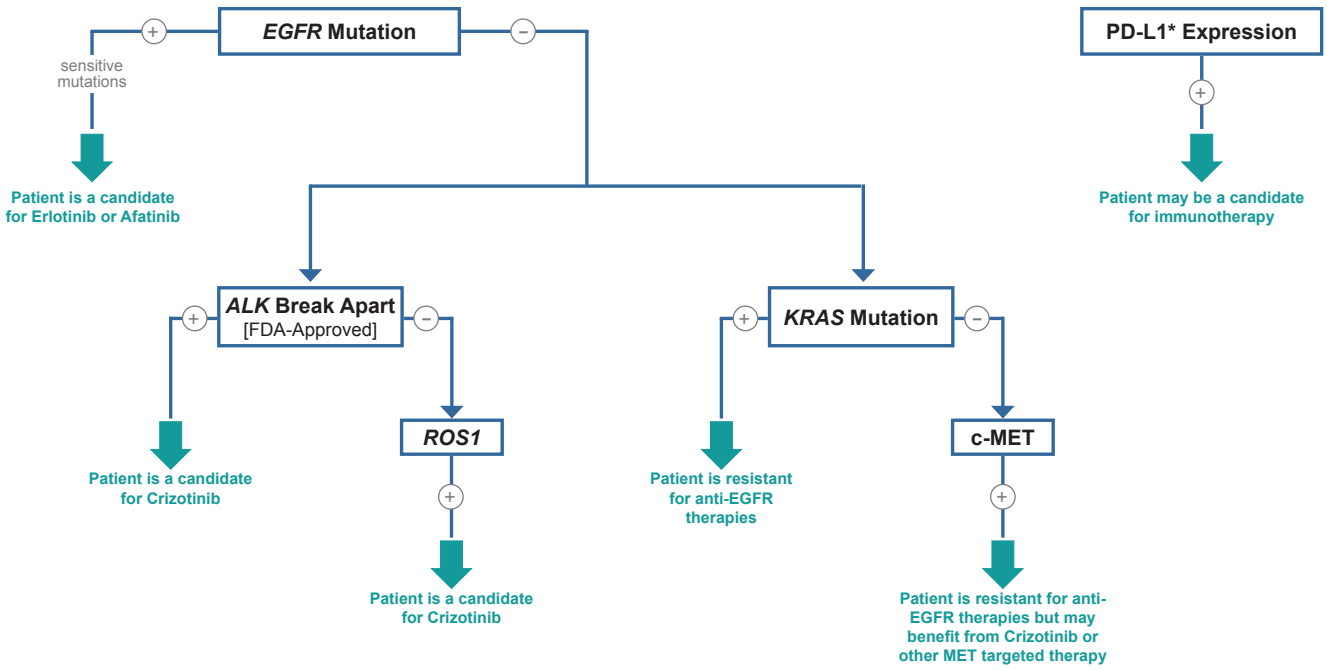
Empowering Personalized Cancer Treatment

LUNG COMPLETE™

Work Up for Lung Complete™

NSCLC Diagnosis & Treatment Monitoring



Note: In addition to *EGFR*, *ALK* Break Apart and *ROS1* testing, *KRAS*, and c-MET testing can be performed to monitor treatment resistance.

* PD-L1 antibody for Research Use Only

This work up is intended as a guide for the comprehensive suite of diagnostic tests included in Lung Complete™ to diagnose and monitor lung cancer. Physicians can order tests individually or allow CGI pathologists and directors to devise a panel evaluation as determined necessary.

Specimen Requirements

	Test	TAT (Mon.-Fri.)	Tissue	Shipping Requirements
Morph. & IHC	**Morphology**	24-48 hours	FFPE block/H&E slide	Room temperature
	IHC Evaluation (c-MET, PD-L1)	24-48 hours	FFPE block or unstained slides	Room temperature
Mol. Dx.	***EGFR* Mutation** [FDA-Approved]	3-5 days	FFPE block or 3-5 sections at 10 µm thickness containing at least 20% of tumor cells evaluated on H&E slides	Room temperature
	***KRAS* Mutation**	5-7 days		
FISH	***ALK* Break Apart** [FDA-Approved]	5-7 days	FFPE block or sections at 3-5 µm thickness on positively coated slides	Room temperature
	***ROS1* DNA FISH Probe**	5-7 days		
Lung Complete™ Panel		10-15 days	FFPE block or 3-5 sections at 10 µm thickness containing at least 20% of tumor cells and 5 sections at 3-5 µm thickness	Room temperature

FFPE: formalin-fixed paraffin-embedded

CGI Laboratory Licensure

CAP (Laboratory #: 7191582, AU-ID: 1434060), CLIA (Certificate #: 31D1038733), New Jersey (CLIS ID #: 0002299), New York State (PFI: 8192), Pennsylvania (031978), Florida (800018142), Maryland (1395), California (COS 800558).

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