City of Hope

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# Assay Summary

## Epidermal Growth Factor Receptor Gene Mutation Analysis

### Responsiveness to EGFR tyosine kinase inhibitors in lung cancer

***Synopsis***

Non-small cell lung cancer (NSCLC) is one of the most common cancers worldwide. Pulmonary malignancies are the leading cause of death in both men and women[1]. Treatment generally consists of surgical resection, radiation therapy and/or chemotherapy. Somatic mutations within the kinase domain (exons 18-21) of the epidermal growth factor receptor (EGFR) gene have been reported for 10-35% of NSCLC tumors[2, 4, 5]. Multiple studies have demonstrated a strong association of EGFR mutation status with response to EGFR tyrosine kinase inhibitors, gefitinib and erlotinib[3, 4, 5, 6].

***Indications for testing***

For patients with a diagnosis of non-small cell lung carcinoma, this test may help predict which cases are likely to benefit from treatment with EGFR tyrosine kinase inhibitors.

***Methodology***

Genomic DNA (gDNA) is extracted from micro-dissected cells from formalin-fixed, paraffin-embedded tissue. A targeted DNA library is generated using the Ion AmpliSeq™ Cancer Hotspot Panel v2 Kit, and sequenced by semiconductor-based next-generation sequencing technology on an Ion Torrent PGM. This test targets 123 hotspot mutations of EGFR, including mutations within exons 18, 19, 20, and 21. Mutations in exons 3, 7, and 15 are also detectable.

***Performance/Limitations***

The gene is not sequenced in its entirety; only the regions including the targeted mutations are analyzed. The method will not detect gross genetic alterations including large deletions, duplications, and inversions. The minimum detectable mutant allele ratio is approximately 10%.

***Specimen Requirements***

**Formalin-fixed, paraffin-embedded (FFPE) tissue blocks or slides.**

The tissue sample should be large enough to provide at least 3000 tumor cells and at least 30% of tumor cells within the tissue.

We prefer to receive formalin-fixed, paraffin-embedded tissue blocks (unused portion will be returned), but slides are also accepted:

- 10 slides, 10 micron serial sections, unstained, without coverslip.
- 1 representative H&E slide, 4 micron section, with a coverslip.
- If the sample is a needle biopsy or clearly has very little tumor, please send additional slides if possible (2 or 3).

- Ensure that the slides are clearly labeled with the patient and sample identifiers and type of sample. Please include a copy of the pathology report.
- Place slides in appropriate container(s) to ensure against breakage.

***Test Request Form (TRF)***

A completed CMDL (TRF) must be submitted with each specimen. Complete testing and billing information must be provided before the specimen is processed

| ***Order Codes*** | ***CPT Codes*** | ***TAT*** |
|---|---|---|
| EGFR-NGS (Targeted analysis for 123 cancer hotspot mutations in the EGFR gene by next generation sequencing) | 81235, 88381, G0452 | 7-14 days |

***References***


1. Ries LAG, Kosary CL, Hankey BF, et al, editors. "SEER Cancer Statistics Review, 1973-1996". Bethesda, MD: National Cancer Institute; 1999.
2. Lynch et al., Activiating Mutations in the Epidermal Growth Factor Receptor Underlying Responsiveness of Non-Small-Cell Lung Cancer to Gefitinib. NEJM, 2004; 350(21): 2129-2139.
3. Fukuoka, M., Yano, S., Giaccone, G., et al., "Multi-institutional randomized phase II trial of gefitinib for previously treated patients with advanced non-small-cell lung cancer., J. Clin. Oncol.;21:2237-46, 2003.
4. Paez et al., EGFR Mutations in Lung Cancer: Correlation with Clinical Response to Gefitinib Therapy. Science, 2004; 304: 1497-1500.
5. Pao et al., EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity of tumors to gefitinib and erlotinib. PNAS, 2004; 101(36): 13306-13311.
6. Pao et al. Acquired resistance of lung adenocarcinomas to gefitinib or erlotinib is associated with a second mutation in the EGFR kinase domain. PLoS Med. 2005 Mar;2(3):e73.