

SOMATIC VARIANT ANNOTATION

**Sample Name** SCLC\_5  
**Date** Sat, Mar 16, 2019  
**Time Processed** 07:00:28 PM

# Clinical Variant #1

**Gene Name** PTEN  
**Protein Change** R233\*  
**Coordinates** chr10:g.89717672C>T  
**ENST ID** ENST00000371953  
**ENSG ID** ENSG00000171862

### Variant Description:

PTEN R233\* has been shown to be a loss of function mutation, and PTEN loss has been the subject of considerable research in breast cancer. PTEN loss may sensitize cells to PI3K-mTOR inhibition. While still being debated, there is data to support that PTEN loss is both associated with poorer prognosis, and no change in prognosis.

### Associated Assertions:

N/A

### Associated Evidence Items:

|  |  |  |
| --- | --- | --- |
| **Description** | **CIViC EID** | **PubMedID** |
| PTEN R233\* Does Not Support Poor Outcome for patients with Glioblastoma Multiforme | EID343 | 22479427 |

# Clinical Variant #2

**Gene Name** EGFR  
**Protein Change** L858R  
**Coordinates** chr7:g.55259515T>G  
**ENST ID** ENST00000275493  
**ENSG ID** ENSG00000146648

### Variant Description:

EGFR L858R has long been recognized as a functionally significant mutation in cancer, and is one of the most prevalent single mutations in lung cancer. Best described in non-small cell lung cancer (NSCLC), the mutation seems to confer sensitivity to first and second generation TKI's like gefitinib and neratinib. NSCLC patients with this mutation treated with TKI's show increased overall and progression-free survival, as compared to chemotherapy alone. Third generation TKI's are currently in clinical trials that specifically focus on mutant forms of EGFR, a few of which have shown efficacy in treating patients that failed to respond to earlier generation TKI therapies.

### Associated Assertions:

1. L858R is among the most common sensitizing EGFR mutations in NSCLC, and is assessed via DNA mutational analysis including Sanger sequencing and next generation sequencing methods. Tyrosine kinase inhibitors erlotinib and gefitinib are associated with improved progression free survival over chemotherapy in EGFR L858R patients. NCCN guidelines recommend (category 1) erlotinib and gefitinib for NSCLC with sensitizing EGFR mutations, along with afatinib and osimertinib.
2. L858R is among the most common sensitizing EGFR mutations in NSCLC, and is assessed via DNA mutational analysis, including Sanger sequencing and next generation sequencing methods. Tyrosine kinase inhibitor afatinib is FDA approved, and is recommended (category 1) by NCCN guidelines along with erlotinib, gefitinib and osimertinib as first line systemic therapy in NSCLC with sensitizing EGFR mutation.

### Associated Evidence Items:

|  |  |  |
| --- | --- | --- |
| **Description** | **CIViC EID** | **PubMedID** |
| EGFR L858R Supports Sensitivity/Response to Gefitinib or Erlotinib for patients with Non-small Cell Lung Carcinoma | EID229, EID275 | 24736073, 24457318 |
| EGFR L858R Supports Sensitivity/Response to Afatinib for patients with Lung Adenocarcinoma | EID879, EID883, EID982 | 23816960, 22452895, 24439929 |
| EGFR L858R Supports Sensitivity/Response to Erlotinib for patients with Non-small Cell Lung Carcinoma | EID885, EID2994, EID2632 | 22285168, 24868098, 15329413 |
| EGFR L858R Supports Sensitivity/Response to Gefitinib for patients with Non-small Cell Lung Carcinoma | EID1665, EID2621 | 18509184, 20038723 |
| EGFR L858R Supports Sensitivity/Response to Gefitinib for patients with Lung Adenocarcinoma | EID2624, EID2634 | 15329413, 22370314 |
| EGFR L858R Supports Resistance to Crizotinib for patients with Non-small Cell Lung Carcinoma | EID4288 | 22235099 |
| EGFR L858R Supports Sensitivity/Response to Erlotinib for patients with Lung Adenocarcinoma | EID4290 | 27032107 |
| EGFR L858R Supports Sensitivity/Response to Afatinib for patients with Non-small Cell Lung Carcinoma | EID2997 | 23982599 |
| EGFR L858R Supports Sensitivity/Response to Dacomitinib for patients with Non-small Cell Lung Carcinoma | EID4860 | 26768165 |
| EGFR L858R Does Not Support Reduced Sensitivity to Gefitinib for patients with Lung Adenocarcinoma | EID6183 | 27022112 |
| EGFR L858R Supports Better Outcome for patients with Non-small Cell Lung Carcinoma | EID347 | 24662454 |

# Processing information

**Variants Processed:** 3  
**Clinical Annotations:** 2

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