VeriStrat Testing for NSCLC TKI Response

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan’s procedure code list for management requirements.

<table>
<thead>
<tr>
<th>Procedure addressed by this guideline</th>
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<td>VeriStrat</td>
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What is VeriStrat testing for non-small cell lung cancer

Definition

The aim of the VeriStrat® test is to help determine which patients with advanced NSCLC may benefit from second-line treatment with an EGFR TKI inhibitor, such as erlotinib, when EGFR mutation status is either negative (wild-type) or unknown.¹

- Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, and is associated with exposure to cigarette smoking.¹
- About 80-85% of NSCLC tumors express the epidermal growth factor receptor (EGFR).¹ EGFR is a cell surface receptor that causes activation of the intracellular tyrosine kinase domain. Overexpression of EGFR results in increased proliferation and survival of cells, leading to the growth of tumors.¹
- Treatment selection in NSCLC may be guided by molecular genetic testing:
  - Approximately 15-25% of patients with NSCLC have activating mutations in the EGFR gene. These patients display improved progression-free survival following treatment with EGFR tyrosine kinase inhibitor (TKI) therapy, such as erlotinib (Tarceva).²³
  - Another 5-7% of patients with NSCLC have the ALK or ROS-1 rearrangements and are treated with crizotinib (Xalkori).⁴
- For the remaining 75-85% of patients, who are negative for both EGFR mutations and ALK/ROS-1 rearrangements, other therapies are used as first-line treatment. However, some of these patients who fail platinum-based chemotherapy or targeted therapies may still benefit from EGFR TKI therapy with erlotinib, which is generally well-tolerated.⁵ This applies in particular to patients whose tumors express an increased number of copies of EGFR (even without EGFR mutations).⁶
Test information

- VeriStrat is a proprietary, serum-based proteomic test using mass spectrometry and bioinformatics to stratify patients into two groups - those expected to have improved survival on EGFR TKI targeted therapy and those who are not expected to have improved survival on EGFR TKI therapy.

- The VeriStrat test result is reported as good, poor, or indeterminate.¹
  - **VSGood results:** patients are candidates for either single-agent chemotherapy or EGFR TKI targeted therapy, such as erlotinib, and may be candidates for multiple lines of therapy.
  - **VSPoor results:** patients are unlikely to benefit from erlotinib and should be considered for single-agent chemotherapy or best supportive care.
  - **Indeterminate results:** In rare instances (< 2%), a test result of indeterminate is reported, indicating that a VSGood or VSPoor classification could not be confirmed.

- VeriStrat is not a replacement for an EGFR mutation test. VeriStrat is designed to determine which patients with negative (wild-type) EGFR mutation status might still benefit from erlotinib since it does have some activity against NSCLC that is EGFR negative.

Guidelines and evidence

- The National Comprehensive Cancer Network (NCCN, 2017) guidelines for the treatment of NSCLC incorporate the use of proteomic tests in the evaluation of therapies for advanced NSCLC. For patients with progression of disease after first-line chemotherapy and good performance status, proteomic testing may help determine which patients may benefit from erlotinib. NCCN guidelines state:¹
  - “Recommend proteomic testing for patients with NSCLC and wild-type EGFR or with unknown EGFR status. A patient with a ‘poor’ classification should not be offered erlotinib in the second-line setting.”

- Demonstration of the clinical utility of VeriStrat testing centers on the results of the PROSE study (2014).⁷ In this prospective, biomarker-stratified, randomized, controlled trial of 263 patients, researchers evaluated the predictive utility of VeriStrat on overall survival (OS) for erlotinib vs. chemotherapy. Key findings include:
  - VSPoor patients had significantly better OS following treatment with chemotherapy vs. erlotinib.
  - VSGood patients demonstrated similar OS when treated with chemotherapy vs. erlotinib.
In the adjusted analysis, VeriStrat classification is predictive of differential OS benefit for erlotinib vs. chemotherapy (HR = 1.85, 95% CI: 1.06-3.24, p=0.031).

A multivariate analysis confirmed VeriStrat classification is independently predictive of OS benefit between erlotinib vs. chemotherapy (p=0.022) when taking confounding variables such as treatment options (chemotherapy vs. erlotinib) smoking history, sex, histology (squamous vs. non-squamous), age, EGFR status and performance status (2 vs. 0 and 1) into account. Performance status was the only other independent predictor aside from VeriStrat.

- Akerley and colleagues (2013) published data regarding physician decision-making based on VeriStrat test results. In this observational analysis, 226 physicians voluntarily submitted pre- and post-test treatment recommendations for 403 VeriStrat tests. Results demonstrated that:
  - Post-test, physicians overwhelmingly recommended erlotinib in 90.3% of VSGood patients vs. 9.6% of VSPoor patients.
  - 90.3% of post-test treatment recommendations correlated positively with test results (i.e., patients with VSGood results received erlotinib while patients with VSPoor results did not).
  - Physicians changed their treatment recommendations following test results in 39.7% of cases.

- Clinical trials involving VeriStrat are currently underway:
  - VeriStrat as Predictor of Benefit of First Line Non Small Cell Lung Cancer (NSCLC) Patients From Standard Chemotherapy (ClinicalTrials.gov identifier NCT02055144)

**Criteria**

- Clinical history
  - Advanced NSCLC, and
  - Good performance status (PS 0-2), and
  - Progression after (or are ineligible for) platinum-based doublet chemotherapy, AND

- Previous genetic testing
  - EGFR testing mutation status is wild-type (negative for an activating mutation)
References


