VeriStrat Testing for NSCLC TKI Response

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v1.0.2020

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 assess prognosis for outcomes in advanced NSCLC and predict survival benefit between EGFR TKIs and single agent chemotherapy.¹

- NSCLC is any type of cancer of the epithelial cells of the lungs that is not classified as small-cell lung cancer.²
- Although associated with cigarette use and smoke exposure, NSCLC can be diagnosed in individuals who have never smoked.²
- About 80-85% of NSCLC tumors express EGFR.³ 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.³,⁴
- 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 TKI therapy, such as erlotinib.⁵,⁶
  - Another 5-7% of patients with NSCLC have the ALK or ROS-1 rearrangements and are treated with crizotinib (Xalkori).⁷
- For the remaining 75-85% of patients, who are negative for both EGFR mutations and ALK or 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

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well-tolerated. This applies in particular to patients whose tumors express an increased number of copies of EGFR (even without EGFR mutations).

**Test information**

- VeriStrat is a proprietary, serum-based proteomic test designed to be an adjunct to a conventional clinical workup, combined with the patient's clinical history, other diagnostic tests, and clinicopathologic factors.
- The VeriStrat test result is reported as good, poor, or indeterminate. The results are also intended to set patient expectations, facilitate a discussion about prognosis, improve knowledge to potentially reduce anxiety, and improve quality of life.
  - **VSGood results:** A good result indicates that a patient is more likely to benefit from standard of care (SOC) treatment and have better overall survival (OS).
  - **VSPoor results:** A poor result indicates that a patient will likely have decreased OS and may benefit from alternative treatment strategies such as novel combination of therapies, NGS testing for rare mutations, non-platinum based regimens, and/or palliative 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.

**Guidelines and evidence**

Previous National Comprehensive Cancer Network (NCCN) guidelines for the treatment of NSCLC supported the use of proteomic tests to evaluate potential therapies in advanced NSCLC. However, likely due to technical advances, availability of next generation sequencing testing for solid tumors, and treatment options, available current NCCN guidelines no longer incorporate these proteomic tests into their NSCLC evaluation algorithms.

- Previous eviCore criteria (VeriStrat Testing for NSCLC TKI Response) were largely based on the 2015 NCCN Guidelines. These recommended proteomic testing for patients with advanced NSCLC who were either EGFR wild type or had an unknown mutation status. For these patients, the NCCN stated that those with a “Poor” result should not be offered second-line erlotinib therapy.
- In contrast, the current 2019 NCCN guidelines for NSCLC no longer include specific recommendations for proteomic testing; there is no mention of proteomic testing or the use of VeriStrat for NSCLC.

**Literature Review**

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The available peer-reviewed clinical validity studies assess the predictive performance of VeriStrat-directed erlotinib therapy compared with chemotherapy in patients who were either EGFR wild type or had an unknown EGFR mutation status and had progressed after first-line treatment. However, 2019 NCCN treatment pathway for patients with NSCLC do not include erlotinib as recommended therapy for patients whose disease has progressed after first-line treatment and are either EGFR wild type or have an unknown mutational status. Since erlotinib is not a recommended therapy, there is no longer a need for a test that can identify it as a treatment option.

The overall evidence base for predictive use is also characterized by several study design limitations. For example, VeriStrat was not used to determine treatment in the available studies and the majority of the study authors reported that treatment selection was based on standard of care. In addition, a “VSGood” result claims to identify NSCLC patients who are EGFR wild-type but still likely to benefit from EGFR-TKI therapy. Yet the clinical validity studies did not consistently test for EGFR variants and, consequently, the true relationship between VeriStrat results, EGFR status, and survival cannot be definitively understood.

For VeriStrat to demonstrate clinical validity in patients with NSCLC in light of the NCCN guideline changes and some of the original design limitations, additional studies supporting its performance are required.

Direct clinical utility studies were not identified in the scientific literature. Examples of these would include prospective studies comparing survival outcomes in patients who had EGFR-TKI treatment selected either by VeriStrat classification or through other standard EGFR variant analysis methods (such as next-generation sequencing).

Regarding the prognostic ability of VeriStrat, the majority of the available evidence predicting disease outcomes included retrospective clinical validity studies which evaluated the test in patients with advanced NSCLC who were treatment-naïve or had either failed first-line treatment or had a recurrence. To infer how well VeriStrat performed as a prognostic test, these studies examined the degree of association between VSGood or VSPoor scores and survival outcomes. Overall, this evidence base demonstrating the performance of VeriStrat as a prognostic test is of low quality.

A number of individual study limitations were observed that weakened the strength of the evidence base. This includes the VeriStrat score not being used to determine treatment and the variability in testing for EGFR variants. Also, the adjustments for EGFR status in survival analyses were inconsistently reported and the relationship between VeriStrat scores and overall survival (OS) as well as progression-free survival (PFS) in study populations with unknown EGFR status was not clear.

Criteria

Given that VeriStrat Testing is not currently supported in clinical practice guidelines for the treatment of advanced NSCLC and the published evidence does not independently
meet the criteria for coverage for this indication, the use of VeriStrat is not considered medically necessary.

- Veristrat is not considered medically necessary and therefore, not eligible for reimbursement.

References


23. Gautschi O, Dingemans AM, Crowe S, et al. VeriStrat(R) has a prognostic value for patients with advanced non-small cell lung cancer treated with erlotinib and