VeriStrat® Proteomic Executive Summary

Despite the launch of national lung cancer screening programs, the latest projections for early stage diagnosis where curative intent is an option is only 16%. [i] A diagnosis of advanced non-small cell lung cancer (NSCLC) represents 70-80% of those diagnosed and it carries a dire prognosis for patients and family members facing this disease For these patients, the goals of treatment are not curative, but are rather to increase the patient's overall survival (OS), improve or maintain quality of life (QOL), and limit the financial burden of care. To achieve these goals, fully characterizing the patients' disease is imperative. The disease state is defined by both tumor characteristics (size, location, anatomy, mutational profile) and the patient's immunological response to the tumor (host response or host biology). The only clinically validated test available for profiling the host response, the VeriStrat® test, is described herein.

The VeriStrat® test is a blood-based proteomic test that identifies a chronic inflammatory immune response indicative of aggressive disease in patients with advanced NSCLC. VeriStrat has historically been known as a predictive test for use of EGFR-TKI inhibitor therapies. Though this predictive utility remains proven, more than 10 years of peer-reviewed, published data has proven to provide critical prognostic information for physicians treating patients with NSCLC. With a binary result of VeriStrat Good (VSGood) or VeriStrat Poor (VSPoor), the test identifies patients with an aggressive immune component to their disease state (VSPoor patients) who are unlikely to respond to standard of care therapies. Patients with a VSGood disease state have an overall survival that is twice as long as those patients who test VSPoor. VeriStrat results are independent of treatment choice, Eastern Cooperative Oncology Group (ECOG) Performance Status (a subjective measure of the patient's mobility), the presence of actionable driver mutations, PD-L1 expression, and other clinical factors (such as age, gender, etc.).[ii,iii,iv,v,vi,vii,viii] Use of this test in real-world clinical practice has been shown to shift physician treatment strategies away from ineffective therapies, resulting in an improvement in OS, quality of life (QOL), and save costs for health plans.[ix,x]

Key Points:

VeriStrat testing provides objective prognostic information independent of therapy choice, mutation status, and other clinical factors, separating patients into two actionable groups:

- VSGood patients have a good overall prognosis in their disease and have been proven to have better response to standard of care therapies independent of other prognostic factors in NSCLC (i.e. ECOG Performance Status, smoking status, EGFR mutation status, KRAS status, PD-L1 expression, and others)[xi,xii]
- VSPoor patients have a poor overall prognosis in their disease and have been proven to have overall survival less than half that of a patient with a VSGood result (HR=0.447), potentially making them better candidates for clinical trials or best supportive care options.

VeriStrat is a blood-based proteomic test that does not require tissue or additional surgical biopsy.

- Provides actionable information to assist physicians in overall treatment strategy. Information is independent of all other clinical prognostic factors including stage, performance status, smoking status and mutation status (e.g. EGFR, KRAS).
- Liquid biopsy and proteomic profiling by mass spectrometry (MALDI-ToF) methodology allow for fast turnaround time to results – 72 hours or less.
- Non-invasive blood test allows avoidance of adverse events and hospitalizations often associated with tissue biopsy for patients with lung cancer.

VeriStrat testing improves OS and QOL for patients while saving on healthcare costs by avoiding ineffective therapy options. [xiii,xiv]

- Following VeriStrat results, 29% of all patients shifted away from treatment with current standard of care therapies in favor of other treatment strategies, including clinical trials or best supportive care (BSC).

- In the VSPoor patient cohort, treatment choices shifted from active therapy to BSC options by 25%, compared to only 1% of patients being considered for BSC prior to receiving the VSPoor test results.
- The test-guided shift in treatment decisions r equates to a cost savings of $6,392 per patient in pharmacy and drug administration spend for health plans. When including the increased costs of surveillance (due to longer OS), hospice referral, change in adverse events management (AE), and the full list price of the test, VeriStrat testing resulted in a total savings of $1,050 per patient.
- In patients with test results of VSPoor (an aggressive disease state) for whom treatment with targeted therapies is ineffective, the cost-saving impact of avoiding ineffective therapies is amplified with a net cost-saving of $10,414 per patient.

Using the VeriStrat test helps physicians participating in the Oncology Care Model (OCM) Medicare payment program meet their quality measures while saving on costs.[xv]

- In-depth literature review shows that traditional prognostic measures are incomplete, and many are subjective (e.g. ECOG performance status). Nevertheless, clinical tests are needed to adequately provide an objective prognosis as required by Medicare payment programs including OCM and Medicare Access and Chip Reauthorization Act of 2015 (MACRA).
- VeriStrat, a robust objective prognostic tool, predicts outcomes and can be used to identify ineffective therapies, avoid costly overtreatment, and facilitating meaningful conversations about overall treatment strategy, such as the timing of best supportive care options including hospice.
- The VeriStrat test significantly improves cancer care planning and quality scores, thereby helping physicians meet the OCM quality measures.

VeriStrat is covered by Medicare and many large commercial health plans

- Local Coverage Determination (LCD) L35396 *Biomarkers for Oncology*[xvi] (formerly L34796 and L33138) reviews the medical necessity of multiple biomarkers and concluded that VeriStrat is medically necessary for patients with NSCLC effective 8/1/2013. Medicare has been reviewing and approving VeriStrat on a case-by-case basis since 2011.
- VeriStrat is covered for commercial beneficiaries by the following national, regional, and state health plans: Cigna, Aetna, Humana, 1199SEIU Benefit Funds, CareFirst BlueCross BlueShield (BCBS), Highmark BCBS, EmblemHealth, Independence BlueCross, BlueCross BlueShield of Michigan, Medical Mutual of Ohio, Health Alliance Plan of Michigan, University of Pittsburgh Medical Center (UPMC) Health Plan, Health Care Service Corp (HCSC consists of BCBS of IL, MT, NM, OK and TX), Florida Blue, AmeriHealth Capital Health Plan , Horizon BCBS of New Jersey, Harvard Pilgrim Health Care, PreferredOne, Group Health Cooperative, and others.

In 84% of cases, NSCLC is diagnosed at an advanced stage when it has largely become incurable. Improved functional status, QOL, and improved OS are significant factors to consider for treatment decisions. New Medicare payment models such as the Oncology Care Model (OCM) also emphasize the importance of improving patient outcomes while decreasing costs by establishing treatment plans and discussing prognosis with patients. By helping to determine the most effective treatment strategy for patients with NSCLC, VeriStrat facilitates decisions for patients classified as VSGood, while enabling those classified as VSPoor to avoid therapies in which they are unlikely to benefit. The VeriStrat test creates an opportunity to decrease drug toxicity, improve QOL, and increase survival outcomes without requiring the use of tissue or a need for re-biopsy.

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