<table>
<thead>
<tr>
<th>Measure Title: Positive PD-L1 Biomarker Expression Test Result Prior to First-Line Immune Checkpoint Inhibitor Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Library ID:</strong></td>
</tr>
<tr>
<td>NQF: N/A</td>
</tr>
<tr>
<td>CLQ: N</td>
</tr>
</tbody>
</table>

**Measure Description:** Percentage of patients, aged 18 years and older, with a diagnosis of metastatic non-small cell lung cancer or squamous cell carcinoma of head and neck on first-line immune checkpoint inhibitor (ICI) therapy, who had a positive PD-L1 biomarker expression test result prior to giving ICI therapy.

**Initial Population:** Patients, 18 years and older, with a diagnosis of metastatic non-small cell lung cancer or squamous cell carcinoma of head and neck and on first-line immune checkpoint inhibitors without chemotherapy.

**Initial Patient Population Guidance:**
- Immune checkpoint inhibitors-class of medications that prevent tumors from “hiding” or “evading” the body’s natural immune system. This is a form of cancer immunotherapy. Immune checkpoint inhibitor medications include PD-1 inhibitor drugs, PD-L1 inhibitor drugs, and CTLA-4 inhibitor drugs.
  - PD-1 inhibitors drugs include: Pembrolizumab, Nivolumab, Cemiplimab
  - PD-L1 inhibitor drugs include: Atezolizumab
  - CTLA-4 inhibitor drugs include: Ipilimumab
- First-line treatment- initial, or first treatment recommended for cancer
- Various treatment regimens were considered, including immune checkpoint inhibitors.
- PD-L1 testing required per FDA approval for the applicable histology
- If the patient is on any of the below immune checkpoint inhibitor(s) as first-line treatment for metastatic disease, they must also have one of the specific subsets of non-small cell lung cancer (NSCLC) or squamous cell carcinoma of head and neck (HNSCC)
  - Pembrolizumab (PD-1 inhibitor drug) AND
    - first-line treatment in patients with metastatic NSCLC OR
    - first-line treatment in patients with metastatic squamous cell carcinoma of the head and neck OR
  - Cemiplimab (PD-1 inhibitor drug) AND
    - first-line treatment in patients with metastatic NSCLC OR
  - Atezolizumab (PD-L1 inhibitor drug) AND
    - first-line treatment in patients with metastatic NSCLC OR
  - Nivolumab (PD-1 inhibitor drug) and Ipilimumab (CTLA-4 inhibitor drug) combination AND
    - first-line treatment in patients with metastatic NSCLC

**Denominator:** Equals Initial Population

**Denominator Exclusions:** Patients with metastatic non-small cell lung cancer (NSCLC) with EGFR or ALK mutations.
**Numerator:** Patients who had a positive PD-L1 biomarker expression test result prior to the initiation of first-line immune checkpoint inhibitor therapy.

**Numerator Guidance:**
- PD-L1 biomarker expression test-FDA approved test that measures the expression of PD-L1 on cancer and/or immune cells.
- Positive PD-L1 biomarker expression test result-PD-L1 test is considered positive if the cancer and/or immune cells have an appropriate threshold of PD-L1 expression based on the approved companion diagnostic.

**Numerator Exclusions:** None

**Denominator Exceptions:** Documentation of medical reason(s) for not performing the PD-L1 biomarker expression test prior to initiation of first-line immune checkpoint inhibitor therapy (e.g., patient is in an urgent or emergent situation where delay to treatment would jeopardize the patient’s health status; other medical reasons/contraindication).

**Denominator Exceptions Guidance:**
- PD-L1 biomarker expression testing was unable to be performed prior to the initiation of first-line immune checkpoint inhibitor therapy due to an urgent or emergent situation where any treatment delay would jeopardize the patient’s health and/or cancer care.
- Lack of available tissue for PD-L1 biomarker expression testing due to a documented medical and/or surgical contraindication which would not allow for the patient to undergo a tissue biopsy safely.

**Stratification/Calculation:** None

**Measurement Period:** Calendar Year

**Clinical Recommendations:**
  Recommendation: The NCCN NSCLC Panel recommends (category 1) IHC testing for PD-L1 expression ideally before first-line treatment (if clinically feasible) in all patients with metastatic NSCLC to assess whether the ICI regimens are an option based on clinical data showing the efficacy of these regimens.

  Recommendation for Recurrent, Unresectable, or Metastatic Disease (non-nasopharyngeal cancers): first-line: Pembrolizumab (for tumors that express PD-L1 with CPS>1) (category 1 if CPS≥20).

**Evidence Strength:**
  Category 1-Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

- Category 1-Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A-Based upon lower-level evidence, there is uniform NCCN consensus that intervention is appropriate.

**Rationale:** Biomarker testing that is not timely may make a difference in treatment decisions and/or patient outcomes. Appropriate treatment delivery could be delayed, or ineffective therapies could be prescribed, resulting in poor clinical outcomes and unnecessary healthcare costs (Pai et al., 2019; Lim et al., 2015).

The NCCN NSCLC Panel emphasizes that clinicians should obtain molecular testing results for actionable biomarkers before administering first-line ICI therapy, if feasible (NCCN Guidelines: NSCLC, 2021).

Despite the ambiguities of PD-L1 testing and definitions, PD-L1 expression may be associated with better outcomes from immunotherapy for recurrent or metastatic HNSCC (ie greater likelihood of response to pembrolizumab and greater survival benefit in response to nivolumab) (NCCN Guidelines: HNSCC, 2021).


**Opportunity for Improvement/Performance Gap:** In 2017, a survey conducted by the Association of Community Cancer Centers (ACCC) reported that only 24% of respondents reported that they had a deep familiarity with checkpoint inhibitors, 32% with monoclonal antibody therapy, and only 17% with combination treatment regimens (ACCC, 2018).

FDA conducted a retrospective analysis in 2017. Patients with clinically-confirmed mNSCLC, diagnosed between January 2011 and March 2016, who had a documented order for, or had been administered, either nivolumab or pembrolizumab, were included in the analyses. PD-L1 expression testing results were abstracted from unstructured data in EHRs. The analysis found that within the first year of FDA approval, 1351 patients with mNSCLC received nivolumab (96.7%), pembrolizumab (3.6%), or both drugs in different lines (0.3%). The median duration of treatment was 113 days (95% CI, 99 to 128 days).
Overall, 11.3% of patients were tested for PD-L1 expression, 42.2% of whom tested positive. An FDA-approved companion diagnostic was used 30.5% of the time. Among patients who received nivolumab, 93.5% were not tested for PD-L1 expression, 2.5% tested positive, and 2.8% tested negative for PD-L1. Among patients who received Pembrolizumab, 37.5% were not tested for PD-L1 expression, 52.0% tested positive, and none tested negative (Dangi-Garimella, 2017).

Results from the first phase of the collaborative MYLUNG Consortium research protocol were based on a retrospective observational chart review of 3,474 adult patients with metastatic NSCLC who initiated first-line systemic therapy within the U.S. Oncology Network practices between April 1, 2018, and March 31, 2020. This study focused on U.S. Oncology Network community practices comprising more than 1,000 providers across the country and found that less than 50% of patients were tested for five major biomarkers (ALK, BRAF, EGFR, PD-L1, and ROS-1) (Robert et al., 2021).

Even though next-generation sequencing is recommended by the National Comprehensive Cancer Network (NCCN) for biomarker testing for patients with non-small cell lung cancer (NSCLC), the uptake among community oncology practices is suboptimal, and the uptake is even lower among Black patients with NSCLC than for White patients (Bruno et al., 2021).


<table>
<thead>
<tr>
<th>Level of Analysis:</th>
<th>Clinician: Group/Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Care Setting:</td>
<td>Outpatient Services</td>
</tr>
<tr>
<td>Data Source:</td>
<td>Registry</td>
</tr>
<tr>
<td>Type of Measure:</td>
<td>Intermediate Outcome</td>
</tr>
<tr>
<td>Interpretation of Score:</td>
<td>Better quality is associated with a higher score</td>
</tr>
<tr>
<td>Intended Use:</td>
<td>Accountability/Public Reporting</td>
</tr>
</tbody>
</table>
Testing:

Feasibility: Five sites using different EHRs and of different affiliations were evaluated in feasibility analysis. While data collected showed that the measure was feasible (with only two data elements not always captured), the provider workflow will have to be modified to fully implement this measure. Overall, full measure implementation presents a slight burden to the providers.

Validity: This measure demonstrated high face validity with 80% of subject matter experts agreeing on the denominator, 80% of subject matter experts agreeing on denominator exclusions, 87% of subject matter experts agreeing on denominator exceptions, and 90% of subject matter experts agreeing on the numerator. Moreover, an average of 72% of subject matter experts agreed that the measure is meaningful, will improve care, addresses a common ailment affecting many patients, and addresses a serious ailment with dangerous consequences.

Reliability: Measure performance scores on one hundred and seventy patients across eleven practices showed high reliability as indicated by an adjusted split-sample correlation coefficient of 0.8513.

For more details, please reach out to measurement@asco.org

Risk Adjustment: None

Telehealth: N/A

Risks to Development/Implementation: FDA approvals for immune checkpoint inhibitor therapy is evolving quickly, as well as the clinical recommendations by clinical guidelines. This measure may need frequent updates in its annual review based on the current evidence and clinical recommendation statements.

Copyright: QPP MIP CQMs (“Registry Measures”) and NQF Copyright Language

The Measure is not a clinical guideline, does not establish a standard of medical care, and has not been tested for all potential applications.

The Measure, while copyrighted, can be reproduced and distributed, without modification, for noncommercial purposes, e.g., use by health care providers in connection with their practices. Commercial use is defined as the sale, license, or distribution of the Measure for commercial gain, or incorporation of the Measure into a product or service that is sold, licensed or distributed for commercial gain.

Commercial uses of the Measure require a license agreement between the user and Society for Immunotherapy of Cancer (SITC) and prior written approval of SITC. Contact info@sitcancer.org for licensing this measure. Neither SITC, the American Society of Clinical Oncology (ASCO), nor its members shall be responsible for any use of the Measure.

ASCO’s significant efforts and contributions to the development of the Measure are acknowledged. SITC is solely responsible for the review and enhancement (“Maintenance”) of the Measure as of January 2022.

SITC encourages use of the Measure by other health care professionals, where appropriate.
REFERENCES:


ADDITIONAL INFORMATION:

None

ORIGINAL APPROVAL DATE:

SITC TEP Approval: 11/15/2021

LAST UPDATED:

SITC TEP: 11/15/2021