CMS Measure ID/CMS QCDR ID: CAP 34

Measure Title: Biomarker Status to Inform Clinical Management and Treatment Decisions in Patients with Non-small Cell Lung Cancer

Measure Specifications

Measure Description	Percentage of non-small cell lung cancer (NSCLC) surgical pathology reports that include anaplastic lymphoma kinase (ALK), epidermal growth factor receptor (EGFR), AND tyrosine protein kinase ROS1 mutation status.
Denominator Statement	All surgical pathology reports with documentation of lung biopsy or resection that have diagnosis of NSCLC CPT©: 88305 (Lung, transbronchial biopsy) 88307 (Lung, wedge biopsy) 88309 (Lung, total/lobe/segment resection) **AND** ICD-10 • C34.00: Malignant neoplasm of unspecified main bronchus • C34.01: Malignant neoplasm of right main bronchus • C34.02: Malignant neoplasm of left main bronchus • C34.10: Malignant neoplasm of upper lobe, unspecified bronchus or lung • C34.11: Malignant neoplasm of upper lobe, right bronchus or lung • C34.12: Malignant neoplasm of upper lobe, left bronchus or lung • C34.2: Malignant neoplasm of middle lobe, bronchus or lung • C34.30: Malignant neoplasm of lower lobe, unspecified bronchus or lung • C34.31: Malignant neoplasm of lower lobe, right bronchus or lung • C34.32: Malignant neoplasm of lower lobe, left bronchus or lung • C34.80: Malignant neoplasm of overlapping sites of unspecified bronchus and lung • C34.81: Malignant neoplasm of overlapping sites of right bronchus and lung • C34.82: Malignant neoplasm of overlapping sites of left bronchus and lung • C34.90: Malignant neoplasm of unspecified part of unspecified bronchus or lung • C34.91: Malignant neoplasm of unspecified part of right bronchus or lung • C34.92: Malignant neoplasm of unspecified part of left bronchus or lung
Denominator Exclusions	Squamous cell carcinoma
Denominator Exceptions	Specimen contains metastatic carcinoma (not a primary neoplasm) Insufficient tissue for testing Necrotic tissue

	No residual carcinoma Not a lung specimen (e.g. lymph nodes, incl hilar lymph nodes; pleural fluid)
Numerator Statement	Surgical pathology reports that contain impression or conclusion of, or recommendation for biomarker mutation testing for each of the three biomarkers, ALK, EGFR and ROS1. Information must be provided about each biomarker; a non-specific note about "biomarker testing" or other documentation that does not conclusively identify each biomarker by name does not meet the measure.
Numerator Exclusions	None
Guidance	This measure is to be reported each time a non-small cell lung cancer specimen pathology report is finalized during the performance period. This measure may be submitted by eligible clinicians who perform the quality actions described in the measure based on the services provided and the measure-specific denominator coding. A short note on mutation status can be made in the final report, such as: • Mutation(s) identified/positive • No mutation(s) identified/ negative • ALK, EGFR and ROS1 testing previously performed • ALK, EGFR and ROS1 mutation testing recommended • ALK, EGFR and ROS1 mutation cannot be determined or is not possible • ALK, EGFR and ROS1 mutation testing not indicated Mutation status may be derived from either the primary or a reference laboratory. The status does NOT have to be the same for all three biomarkers as long as each is recorded.
Measure Information	
NQS Domain	Communication and Care Coordination
Meaningful Measures Area(s)	Transfer of Health Information and Interoperability
Meaningful Measure Rationale	Various gene alterations have been identified as oncogenic drivers for NSCLC, including mutations of EGFR, ALK and ROS1. The Lung Cancer Mutation Consortium found that two thirds of NSCLC patients have an oncogenic driver and that overall survival improves if patients receive matched targeted therapy (1). Referring physicians depend on both the pathologists' interpretations of and any recommendations for tests in order to provide quality patient care. If the status is not indicated in each pathology report for the patient, unnecessary repeat testing may be performed delaying treatment and increasing cost. This

measure monitors the success of pathologists in effectively communicating this important information for the purpose of care coordination and efficient use of resources.

Knowledge of mutation status of ROS1, ALK and EGFR is thus necessary for appropriate clinical decision-making in advanced NSCLC. Alternative treatments are considered when any one or more of these rearrangements are discovered before or during first-line chemotherapy. ROS1 rearrangement occurs in 1% to 2% of non-small cell lung carcinomas and predicts response to crizotinib and ceritinib therapy, which are first-line treatments. Response rates, including complete responses, approach 70% (2-4). For ALK1, in addition to identifying tumors that are likely to respond to targeted therapies, knowledge of ALK rearrangement status typically predicts inferior response to immunotherapies. Approximately 5% of lung adenocarcinomas have a chromosomal rearrangement involving the ALK gene and associated with ALK protein overexpression. Patients with such tumors respond to therapy with ALK tyrosine kinase inhibitors, such as crizotinib (2, 5). Finally, approximately 20% of lung adenocarcinomas contain an EGFR activating mutation that predicts response to therapy with EGFR tyrosine kinase inhibitors such as erlotinib (2, 6-10).

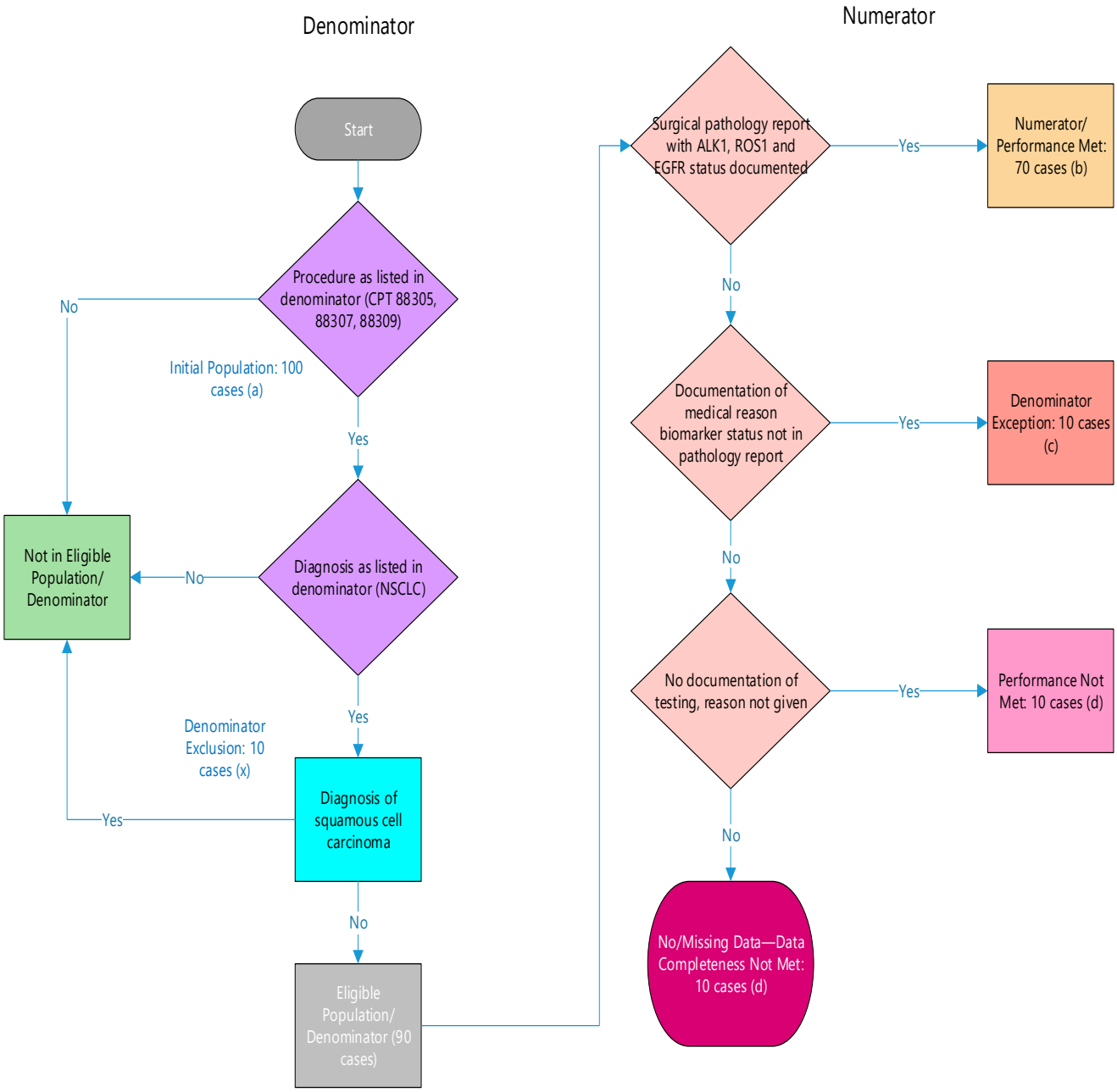
1. Kris MG, Johnson B, Berry LD, et al. Using multiplexed assays of oncogenic drivers in lung cancers to select targeted drugs. JAMA. 2014;311:1998–2006.
2. Lindeman NI, Cagle PT, Aisner DL, Arcila ME, Beasley MB, Bernicker EH, et al. Updated molecular testing guideline for the selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors: Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. J Thorac Oncol. 2018 Mar;13(3):323-358.
3. Takeuchi K, Soda M, Togashi Y, et al. RET, ROS1 and ALK fusions in lung cancer. Nat Med. 2012;18(3):378-381.
4. Bergethon K, Shaw AT, Ou SH, et al. ROS1 rearrangements define a unique molecular class of lung cancers. J Clin Oncol. 2012;30(8):863-870.
5. Shaw AT, Kim DW, Nakagawa K, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. N Engl J Med. 2013;368(25):2385-2394.
6. Maemondo M, Inoue A, Kobayashi K, et al. Gefitinib or chemotherapy for non-small-cell lung cancer with mutated EGFR. N Engl J Med. 2010;362(25):2380-2388.
7. Mitsudomi T, Morita S, Yatabe Y, et al. Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial. Lancet Oncol. 2010;11(2):121-128.

	8. Mok TS, Wu YL, Thongprasert S, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009;361(10):947-957. 9. Pao W, Miller V, Zakowski M, et al. EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity of tumors to gefitinib and erlotinib. Proc Natl Acad Sci. 2004;101(36):13306-13311. 10. Rosell R, Carcereny E, Gervais R, et al. Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial. Lancet Oncol. 2012;13(3):239-246
Measure Type	Process
Data Source	Laboratory Information Systems; pathology reports
Summary of Performance Gap Evidence	For performance year 2021, 15 reporting entities submitted data on this measure to CMS, although four were below the 20-case minimum. Case numbers ranged from 9 to 500. Performance scores ranged from 0% to 100% with an average performance of 62.56%. For January 1st to July 1st 2022, 7 reporting entities have entered data into the Pathologists Quality Registry for this measure. Case numbers range from 4 to 314. Performance scores range from 80% to 100% with an average score of 96%. Although ROS1 rearrangement predicts response to first line treatments, testing for ROS1 rearrangements occurs in as few as 20.6% of NSCLC cases or as many as 28% of cases (average 27.5%) (1, 5). Testing rates of ALK are higher, but recent study indicated as few as 58-64% of cases were tested for ALK rearrangement (1, 2, 5). Possibly due to the higher rate of EGFR mutation as compared to ROS1 or ALK rearrangement, rates of testing for EGFR mutation are higher than either ROS1 or ALK at approximately 75% (3), although EGFR testing varies depending on cancer stage (5). Testing rates also vary across institutions and institution types. A 2021 study of sites in The US Oncology Network, which represents over 450 community oncology practices, found documentation of biomarker testing in the EHR was available in 35.5% of patients for EGFR, 32.9% for ALK, 5.7% for ROS1 (6) Data regarding testing of all three mutation together are not as widely available, as ROS1 testing in particular has only recently been seen as standard. However, one study from 2019 indicated that 15.4% (875 out of 5688) of NSCLC patients who were tested for biomarkers received multigene panel sequencing (4).

	1. Budget Impact of Next-Generation Sequencing for Molecular Assessment of Advanced Non–Small Cell Lung Cancer. (2018) Yu, Tiffany M. et al. Value in Health, Volume 21, Issue 11, 1278 – 1285 2. LungCARD-Report on worldwide research and clinical practices related to lung cancer (2019) Jankovic, R et al JBUON 24(1): 11-19 3. The Clinical and Economic Impact of Inaccurate EGFR Mutation Tests in the Treatment of Metastatic Non-Small Cell Lung Cancer (2017) Cheng MM et al. J. Pers. Med.7(3), 5 4. Cost Effectiveness of Multigene Panel Sequencing for Patients With Advanced Non–Small-Cell Lung Cancer. (2019) Steuten L et al. JCO Clinical Cancer Informatics 3, 1-10 5. Pennell NA, Arcila ME, Gandara DR, West H. Biomarker Testing for Patients With Advanced Non-Small Cell Lung Cancer: Real-World Issues and Tough Choices. Am Soc Clin Oncol Educ Book. 2019 Jan;39:531-542. 6. Understanding Contemporary Molecular Biomarker Testing Rates and Trends for Metastatic NSCLC Among Community Oncologists Waterhouse DM, Tseng W-Y, Espirito JL and Robert NJ (2021) Clinical Lung Cancer, Volume 22, Issue 6, e901 - e910
Measure Owner	College of American Pathologists
NQF ID	N/A
Number of Performance Rates	1
Overall Performance Rate	1st Performance Rate
High-priority	Yes
Improvement Notation	Inverse Measure: No **Proportional Measure: Yes (Higher score indicates better quality)** Continuous Variable Measure: No Ratio Measure: No Risk-adjusted: No
Care Setting and Specialty	Care Setting: Other—Laboratories; Telehealth not applicable Specialty: Pathology
Submission Pathway	Traditional MIPS Only
Current Clinical Guideline the Measure is Derived From	ROS1 testing must be performed on all lung advanced-stage adenocarcinoma patients, irrespective of clinical characteristics (Strong Recommendation) (1). The NCCN guideline for non-small cell lung cancer recommends testing for ROS1 rearrangements for nonsquamous NSCLC or NSCLS NOS (Category 2A evidence) (2).

	ALK molecular testing should be used to select patients for ALK-targeted TKI therapy, and patients with lung adenocarcinoma should not be excluded from testing on the basis of clinical characteristics (Grade B evidence) (3). Testing for ALK gene rearrangements and EGFR gene mutations is recommended in the NSCLC algorithm for patients with nonsquamous NSCLC or NSCLC NOS so that patients with these genetic abnormalities can receive effective treatment with targeted agents (Category 1 evidence) (2). EGFR molecular testing should be used to select patients for EGFR-targeted TKI therapy, and patients with lung adenocarcinoma should not be excluded from testing on the basis of clinical characteristics (Grade A Evidence) (3). EGFR mutation testing should be ordered at the time of diagnosis for patients presenting with advanced-stage disease (stage IV according to the 7th edition TNM staging system) who are suitable for therapy or at time of recurrence or progression in patients who originally presented with lower-stage disease but were not previously tested (Grade A Evidence) (3). Physicians may use molecular biomarker testing in tumors with histologies other than adenocarcinoma when clinical features indicate a higher probability of an oncogenic driver (Expert Consensus Opinion) (1, 2). 1. Lindeman NI, Cagle PT, Aisner DL, Arcila ME, Beasley MB, Bernicker EH, et al. Updated molecular testing guideline for the selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors: Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. J Thorac Oncol. 2018 Mar;13(3):323-358. 2. Ettinger DS, Wood DE, Aisner DL, Akerley W, Bauman J, Chang JY, et al. NCCN clinical practice guidelines in oncology: non-small cell lung cancer, version 3.2022. National Comprehensive Cancer Network. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf 3. Lindeman NI, Cagle PT, Beasley MB, Chitale DA, Dacic S, Giaccone G, et al. Molecular testing guideline for selection of lung cancer patients for EGFR and ALK tyrosine kinase inhibitors: guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology. Arch Pathol Lab Med. 2013 Jun;137(6):828-60.

Measure Flow



SAMPLE CALCULATION:

$$\frac{\text{Numerator (b=70 reports)}}{\text{Denominator (a=100 cases)-Denominator Exclusions (x=10 cases)-Denominator Exceptions (c=10 cases)}} = 87.5\%$$