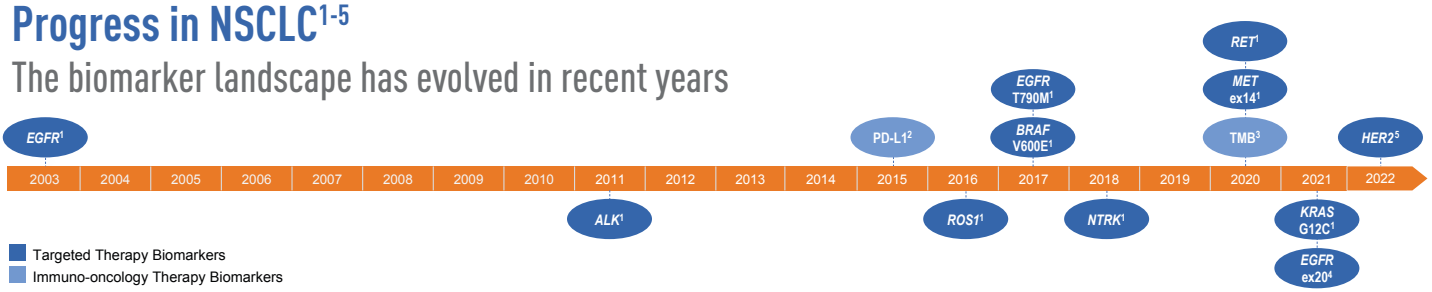
NON-SMALL CELL LUNG CANCER (NSCLC)
BIOMARKER TESTING LANDSCAPE

Progress in NSCLC[1-5]

The biomarker landscape has evolved in recent years

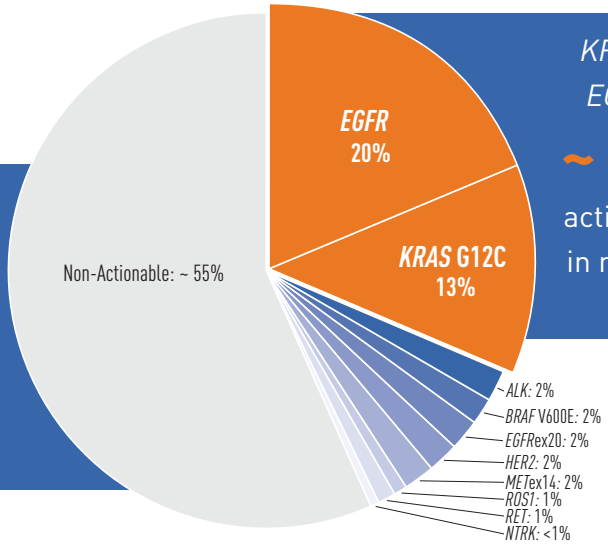


- **More than 20 targeted therapies** have been approved **for use in NSCLC**[1]
- **~ 60% of cancer therapies** launched in the US between 2015 and 2020 **require or recommend biomarker testing prior to use**[6]

Prevalence of Actionable Oncogenic Drivers in NSCLC*

~ 2 in every 5

patients with non-squamous NSCLC have an actionable driver mutation[7]



KRAS G12C and *EGFR* make up **~ 75%** of all actionable drivers in non-squamous NSCLC[7]

*Molecular alteration prevalence can vary slightly between different datasets and studies. Values in the graph are based on approximate molecular alteration frequencies from the AACR GENIE version 12.0 dataset (N=19,777). Participating institutions include academic centers in western countries. This graph only includes alterations predictive of response to an FDA-approved drug in locally advanced or metastatic NSCLC.[7]

Guidelines Recommend Broad Molecular Testing for Eligible Patients With Advanced NSCLC[8-10]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Recommendations[8,†,‡]

Actionable	Molecular Biomarker									Immune Biomarker	Emerging	Molecular Biomarker
	EGFR	*KRAS* G12C	*ALK*	*HER2*	*MET*ex14	*BRAF*	*ROS1*	*RET*	*NTRK1/2/3*	PD-L1		*MET*amp

Testing should be conducted as part of a broad molecular profiling | Single-biomarker immunohistochemistry testing recommended | Expanded-panel testing recommended

†The NCCN Guidelines® for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.[8]

‡The NCCN Guidelines for NSCLC recommend broad molecular testing to identify rare driver variants for which targeted therapies may be available to ensure patients receive the most appropriate treatment.[8]

- **ASCO and CAP/AMP/IASLC guidelines recommend testing for actionable and emerging biomarkers utilizing a comprehensive panel or targeted testing**[9,10]

AACR, American Association for Cancer Research; ALK, anaplastic lymphoma kinase; AMP, Association for Molecular Pathology; ASCO, American Society of Clinical Oncology; BRAF, proto-oncogene B-Raf; CAP, College of American Pathologists; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; IASLC, International Association for the Study of Lung Cancer; KRAS, Kirsten rat sarcoma; MET, mesenchymal-to-epithelial transition; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; NTRK, neurotrophic tyrosine receptor kinase; PD-L1, programmed cell death ligand 1; RET, rearranged during transfection; ROS1, c-ros oncogene 1; TMB, tumor mutational burden.

Guideline-Recommended Biomarker Testing May Improve Patient Outcomes[11,*,†]

Adherence to testing for guideline-recommended biomarkers, regardless of therapy

Decreased mortality risk by **11%**

*This was a retrospective study of 28,784 patients diagnosed with advanced NSCLC. Adherence to biomarker testing consisted of patients with evidence of testing for any biomarker, including *EGFR*, *ALK*, *BRAF*, *KRAS*, *ROS1*, or PD-L1 between 14 days prior to and 90 days after diagnosis of advanced NSCLC and the main outcome, overall survival (OS), was agnostic to treatment.[11]

†Multivariable analysis was adjusted for age at diagnosis of advanced NSCLC, sex, smoking status, and stage at initial diagnosis of NSCLC.[11]

Many Patients With Newly Diagnosed NSCLC Do Not Receive Broad Molecular Testing[12]

~ 50% of metastatic patients received comprehensive biomarker testing[12,‡]

Regardless of patient characteristics such as age, race, and smoking status, **biomarker testing** should be conducted in **all eligible patients** with advanced NSCLC[13]

‡A retrospective, observational study assessing real-world biomarker testing patterns in 3,474 patients with metastatic NSCLC from community oncology practices within The US Oncology Network between 2018 and 2020.[12]

Obtaining Prior Biomarker Test Results Can Be Challenging[14,15]

In an Amgen sponsored survey of 196 oncologists who planned to use biomarker test results obtained at diagnosis to inform 2L+ treatment decisions, ~2/3 faced one or more of the following obstacles[15,§]:

Previous biomarker test results are lost[15,16]	Process for obtaining previous results is complex[14,15]	EMR test results are not in an easily accessible format[13,15]	Cannot access prior test results from patient referrals[15,16]	Retrieving medical records from other physicians[15,16]

§Data from a 30 minute double-blind online survey of 196 oncologists (n=55 academic, n=141 community) performed between Jan 1, 2022 and March 31, 2022.[15]

Biomarker Testing Considerations

Addressing Tissue Insufficiency

- Next-generation sequencing can reduce the number of ordered assays and conserve tissue[13]
- Rapid On-Site Evaluation (ROSE) assesses sample adequacy for molecular diagnostic studies, potentially reducing rebiopsy rates[17]
- Tissue biopsy is the gold standard for biomarker testing; however, using cfDNA in addition to tissue resulted in a 48% increase in the identification of patients with a guideline-recommended biomarker[18,**]
- Liquid biopsy can be used when tissue collection is not feasible or test results are unavailable[18,19]
- Due to false negative rates reflexing to tissue is recommended[19]

Shortening Turnaround Time (TAT)

- Broad molecular testing at diagnosis may take less time than consecutive single-gene testing, a process of elimination approach[20]
- Reflex testing protocols can reduce average TAT by 37 days[21]

Considerations for Consistent Reporting

- Include all actionable mutations at the beginning of the report[22]
- Report all mutations at the variant level[22]
- Use uniform and unambiguous nomenclature to report variants (ie, *KRAS* G12C)[22]

Documenting and Retrieving Biomarker Results

- Append patients' biomarker test reports in a reliable location within their EMR, such as with their surgical pathology report[23,24]
- Consider establishing the optimal location for test results with your multidisciplinary team for easy retrieval by providers, now and in the future[23]

**In the NILE study of 282 patients with non-squamous mNSCLC who received SOC tissue genotyping and cfDNA analysis for guideline-recommended biomarkers between 2016 and 2018. Overall concordance across four genes (*EGFR* exon 19 deletion and L858R, *ALK* fusion, *ROS1* fusion, and *BRAF* V600E).[18]

Learn more at FindKRASG12C.com

2L, second line; cfDNA, circulating-free DNA; EMR, electronic medical record; mNSCLC, metastatic non-small cell lung cancer; SOC, standard-of-care.

References: **1.** Majeed U, et al. *J Hematol Oncol*. 2021;14:108. **2.** National Institutes of Health. www.cancer.gov. Accessed November 28, 2022. **3.** Food and Drug Administration. www.fda.gov. Accessed November 28, 2022. **4.** Food and Drug Administration. www.fda.gov. Accessed November 28, 2022. **5.** Food and Drug Administration. www.fda.gov. Accessed November 28, 2022. **6.** IQVIA Institute. www.iqvia.com. Accessed November 28, 2022. **7.** Data on file, Amgen; [Analysis of AACR Genie v12]. **8.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer v.1.2023. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed January 9, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **9.** Lindeman NI, et al. *Arch Pathol Lab Med*. 2018;142:321-346. **10.** Hanna NH, et al. *J Clin Oncol*. 2021;39:1040-1091. **11.** John A, et al. *Adv Ther*. 2021;38:1552-1566. **12.** Robert N, et al. Presented at: American Society of Clinical Oncology Annual Meeting; June 4–8, 2021; Virtual Meeting. Abstract 9004. **13.** Pennell NA, et al. *Am Soc Clin Oncol Educ Book*. 2019;39:531-542. **14.** Schilsky RL, et al. *N Engl J Med* 2022; 387:2107-2110. **15.** Data on file, Amgen; [Physician ATU]. **16.** Foley KA, et al. *Val Outcomes Spot*. 2015;6-9. **17.** Ofiara LM, et al. *Front Oncol*. 2014;4:253. **18.** Leighl NB, et al. *Clin Cancer Res*. 2019;25:4691-4700. **19.** Rolfo C, et al. *J Thorac Oncol*. 2018;13:1248-1268. **20.** Pennell NA, et al. *JCO Precis Oncol*. 2019; 3:1-9. **21.** Anand K, et al. *Clin Lung Cancer*. 2020;21:437-442. **22.** Li MM, et al. *J Mol Diagn*. 2017;19:4-23. **23.** Kim ES, et al. *J Thorac Oncol*. 2019;14:338-342. **24.** National Cancer Institute. https://www.cancer.gov. Accessed April 10, 2023.

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