

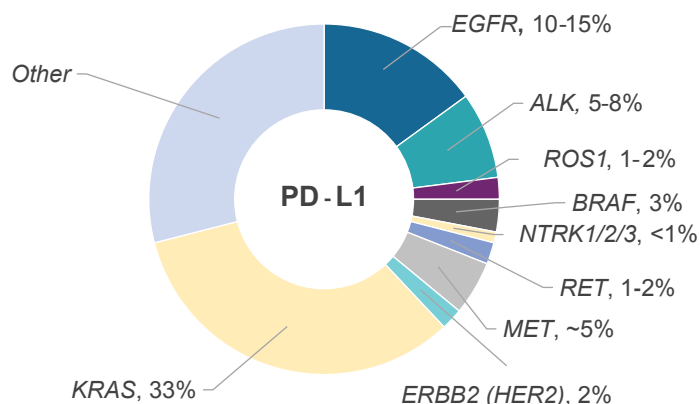
Next-Generation Sequencing:

A Comprehensive Biomarker Testing Approach in NSCLC



The NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) for NSCLC strongly advises broader molecular profiling with the goal of identifying rare driver mutations for which effective drugs may already be available^{1-12,a}

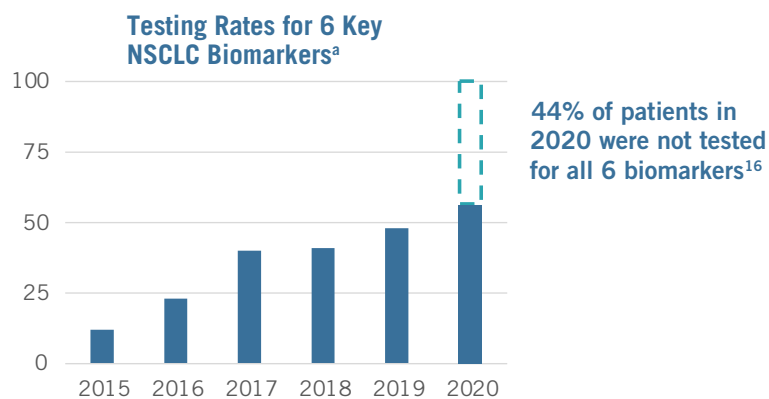
- NGS can detect multiple actionable and emerging biomarkers in a single test¹³
- Given the large prevalence of actionable biomarkers in NSCLC, comprehensive panel testing using NGS may be an optimal method of biomarker testing in NSCLC^{14,15}



^aThe NCCN Guidelines® for NSCLC provide recommendations for individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.

Real-World Data Show That Not All Patients With Advanced NSCLC Are Being Tested for All Actionable Biomarkers¹⁶

A retrospective medical record review examined the extent of biomarker testing in patients with advanced or metastatic NSCLC (N=3,860) within a network of community practices¹⁶



^aThe 6 biomarkers analyzed in this study were the following: *ALK*, *BRAF*, *EGFR*, *KRAS*, *PD-L1*, and *ROS1*.

NGS May Offer an Efficient, Comprehensive Approach to Biomarker Testing¹⁷⁻¹⁹



Account for multiple biomarkers with 1 test



Fewer rebiopsies and complications



Shorter time-to-test results



Lower costs to healthcare system

NGS may offer many benefits, including greater efficiency, cost-effectiveness, and decreased time for results than other biomarker testing methods^{15,19}

When testing for biomarkers, evaluate NGS against other methods

Different NGS Assays Are Available for Biomarker Testing Across Tumor Types



Here are several examples of NGS assays that can use liquid biopsies or tissue biopsies^{a,b}

Assays ²⁰⁻²⁸	Guardant360® CDx ^c	FoundationOne® CDx and Liquid CDx ^d		Oncomine™ Dx Target Test ^e	LDTs (Non-FDA-approved)
Description	Provides tumor mutation profiling for 55 genes	Liquid CDx: profiles >300 genes and select biomarkers (including PD-L1)	CDx: Profiles >300 genes and genomic signatures	Detects sequence variations in 23 genes	Varies in number of genes detected
Tissue type	Liquid only	Liquid only	Tissue only	Tissue only	Tissue or liquid
FDA-approved CDx biomarkers	EGFR mutations, KRAS G12C, and more	ALK rearrangements, EGFR mutations, and more	ALK rearrangements, BRAF V600E, and more	ROS1, BRAF V600E, EGFR mutations, and more	N/A

^aThere is a growing number of FDA-approved NGS assays, and this slide does not cover all of them. See list of FDA-approved assays for more information.²⁹ ^bThis chart is for illustrative purposes only. Genentech does not endorse or recommend any specific commercial assay. ^cGuardant360® CDx is a trademark of Guardant Health, Inc. ^dFoundationOne® is a trademark of Foundation Medicine, Inc. ^eOncomine™ Dx is a trademark of Life Technologies Corporation.

ASCO guidelines state that all patients with metastatic or advanced cancer should undergo biomarker testing in a certified laboratory with multigene panel-based assays for cancers with >1 approved biomarker-driven therapies³⁰

NGS Coverage and Patient OOP Costs Vary Based on Insurance Types

Medicare ^{31,32}	 Commercial Insurer ³³⁻³⁵	 Medicaid ³²⁻³⁵	DoD ³⁶⁻³⁷
<ul style="list-style-type: none"> Covers all FDA-approved oncology NGS tests Some MACs have issued additional local coverage decisions May not cover 100% of patient OOP costs 	<ul style="list-style-type: none"> Variable coverage for NGS testing—many plans do cover NGS May require a prior authorization Variability in patient OOP costs 	<ul style="list-style-type: none"> Each Medicaid program has different coverage and patient OOP costs 	<ul style="list-style-type: none"> The DoD covers NGS testing through an agreement with a national reference lab^a Coverage varies by plan, patient diagnosis, and other factors

^aThe DoD covers NGS testing through agreements with Foundation Medicine, Inc.

There is more work to be done to make NGS testing widely available, accurate, and covered by payers¹⁴

To learn more about comprehensive biomarker testing for metastatic NSCLC, please visit www.biomarkertesting.com

ALK = anaplastic lymphoma kinase; BRAF = v-Raf murine sarcoma viral oncogene homolog B1; CDx = companion diagnostic; DoD = Department of Defense; EGFR = epidermal growth factor receptor; ERBB2 = erb-b2 receptor tyrosine kinase 2; FDA = Food and Drug Administration; HER2 = human epidermal growth factor receptor 2; KRAS = Kirsten rat sarcoma 2 viral oncogene homolog; LDT = laboratory developed tests; MAC = Medicare Administrative Contractor; NCCN = National Comprehensive Cancer Network; NSCLC = non-small cell lung cancer; NGS = next-generation sequencing; NTRK = neurotrophic tyrosine receptor kinase; OOP = out-of-pocket; PD-L1 = programmed death-ligand 1; RET = rearranged during transfection; ROS1 = c-ros oncogene1.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V3.2022. © National Comprehensive Cancer Network, Inc., 2022. All rights reserved. Accessed May 4, 2022. 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. 2. Kris MG, et al. *JAMA*. 2014;311:1998-2006; 3. American Cancer Society. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf>. Accessed September 16, 2021; 4. Cancer Genome Atlas Research Network. *Nature*. 2014;511:543-550; 5. Davies H, et al. *Nature*. 2002;417:949-954; 6. Bartholomew C, et al. *Respir Med Case Rep*. 2017;20:137-140; 7. Farago AF, et al. *JCO Precis Oncol*. 2018;2018:PO.18.00037; 8. Kim H, Chung JH. *Transl Lung Cancer Res*. 2015;4:149-155; 9. Heist RS, et al. *Oncologist*. 2016;21:481-486; 10. Teixido C, et al. *Ther Adv Med Oncol*. 2018;10:1758835918763493; 11. Li BT, et al. *J Clin Oncol*. 2018;36:2532-2537; 12. Li BT, et al. *J Clin Oncol*. 2018;36:2532-2537; 13. Reitsma M, et al. *J Mang Care Spec Pharm*. 2019;25:601-611; 14. International Association for the Study of Lung Cancer. <https://www.iaslc.org/iaslc-news/filcn/time-end-debate-genomic-testing-nscll>. Accessed September 29, 2021; 15. Pennell NA, et al. *JCO Precis Oncol*. 2019;3:1-9; 16. Vanderwalde AM, et al. *J Clin Oncol*. 2021;39(28 suppl):287; 17. Lindeman NJ, et al. *Arch Pathol Lab Med*. 2018;142:321-346; 18. Pennell NA, et al. *Am Soc Clin Oncol Educ Book*. 2019;39:531-542; 19. Dall'Olio FG, et al. *Lung Cancer*. 2020;149:5-9; 20. Guardant360 CDx. <https://guardant360cdx.com/genelist/>. Accessed August 23, 2021; 21. Guardant360 CDx. <https://guardant360cdx.com/wp-content/uploads/2021/06/D-001590-Guardant360-CDx-Technical-Information-Document-R1.pdf>. Accessed August 23, 2021; 22. Foundation Medicine. <https://www.foundationmedicine.com/test/foundationone-liquid-cdx>. Accessed July 7, 2021; 23. Foundation Medicine. https://assets.ctfassets.net/w98cd481qyp0/6LDQZQEQLvWD4Kj1lXKo5/d4edef9488124167e463da024ce29f71/NSCLC_Profiler.pdf. Accessed August 23, 2021; 24. Foundation Medicine. http://info.foundationmedicine.com/hubfs/FMI%20Labels/FoundationOne_Liquid_CDx_Label_Technical_Info.pdf. Accessed August 23, 2021; 25. Foundation Medicine. <https://www.foundationmedicine.com/test/foundationone-cdx>. Accessed October 21, 2021; 26. ThermoFisher Scientific. <https://www.thermofisher.com/order/catalog/product/A32451>. Accessed December 5, 2021; 27. Goodsaid FM. *Clin Transl Sci*. 2019;12:431-439; 28. Schwartzberg LS, et al. *NPI Precis Oncol*. 2020;4:15; 29. US Food and Drug Administration. <https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools>. Accessed October 21, 2021; 30. Chakravarty D, et al. *J Clin Oncol*. 2022;40:1231-1258; 31. Center for Medicare and Medicaid Services. <https://www.cms.gov/medicare-coverage-database/view/nccalc-decision-memo.aspx?proposed=N&NCAId=296>. Accessed October 20, 2021; 32. Phillips KA. *JAMA*. 2018;319:2379-2380; 33. Lu CY, et al. *J Pers Med*. 2018;8:19; 34. LUNGevity. https://www.lungevity.org/sites/default/files/biomarker/ACS-CAN_LUNGevity_PayerCoveragePoliciesofTumorBiomarkerTesting_112018.pdf. Accessed December 7, 2021; 35. Grant P, et al. *Clinical Genetics*. 2021;100:504-521; 36. TRICARE Cancer Clinical Trials. <https://tricare.mil/Plans/SpecialPrograms/CancerClinicalTrials>. Accessed December 3, 2021; 37. Foundation Medicine. <https://www.foundationmedicine.com/press-releases/d094da4f-e0c4-4f10-9dfe-a5a10da67007>. Accessed December 3, 2021.