Updates are needed in HER2 (*ERBB2*)-mutant mNSCLC

Further research into HER2 (*ERBB2*)-mutant mNSCLC could expand the understanding of the disease

Boehringer Ingelheim

HER2=human epidermal growth factor receptor 2; mNSCLC=metastatic non-small cell lung cancer.

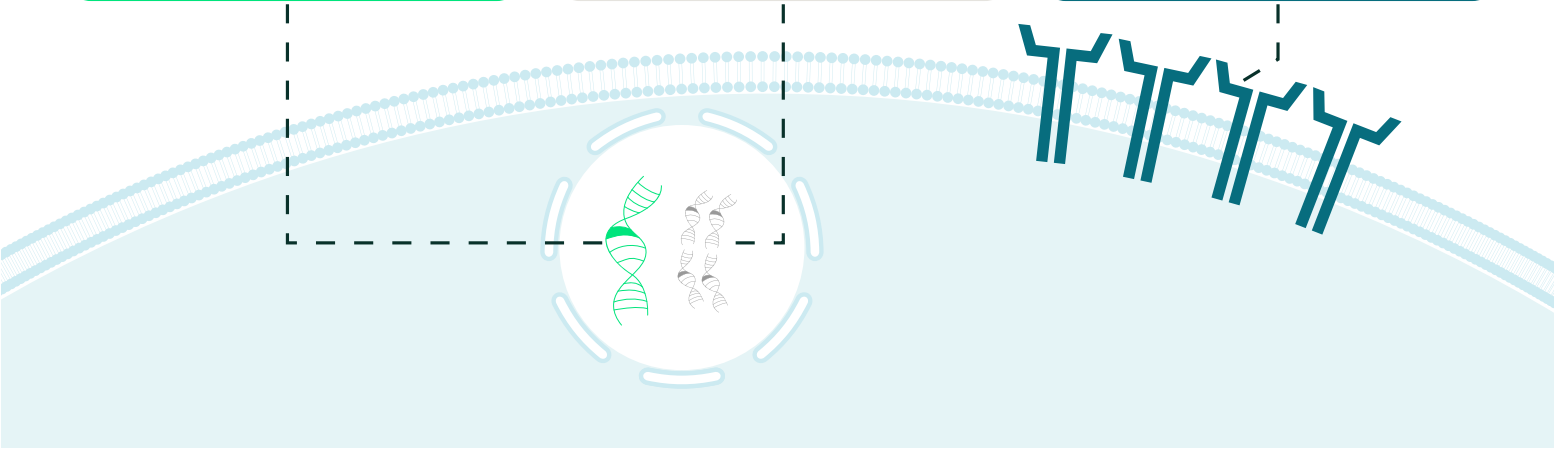
Mutations in HER2 (*ERBB2*) play a significant role in NSCLC[1]

This contrasts with amplification and overexpression, which are main drivers in other cancers[1]

HER2 mutations	
Frequency	2-4%[2]
Result	Alterations in the sequence of the HER2 gene in the genome[3]
Significance	Increased invasiveness and tumorigenicity[2]
Detection	NGS; RT-PCR[1,3]

HER2 amplification	
Frequency	2-4%[2]
Result	Increased number of gene copies[3]
Significance	Increased HER2 protein expression and signaling[2]
Detection	FISH[3]

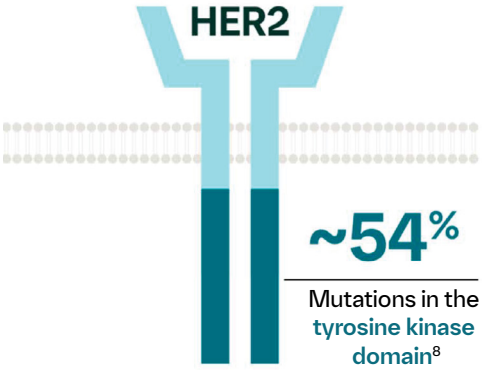
HER2 overexpression	
Frequency	3-34%[2]
Result	Increased HER2 receptor expression and dimerization[2,3]
Significance	Increased pathway activation, promoting cell proliferation[4]
Detection	Immunohistochemistry[3]



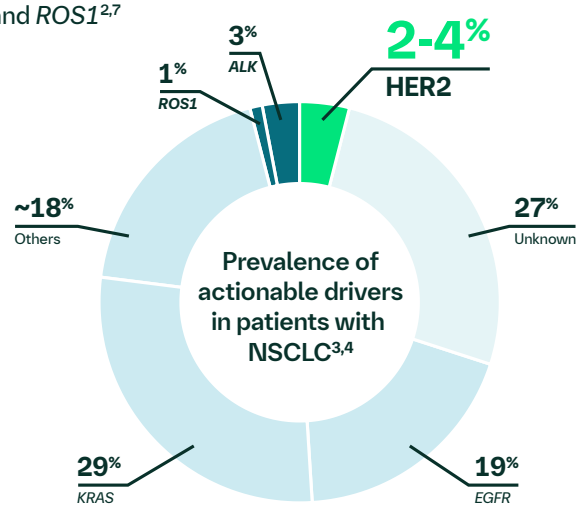
HER2 (*ERBB2*) mutations have emerged as actionable drivers in NSCLC[5]

HER2 mutations are often mutually exclusive to established oncogenic drivers, such as *EGFR* (*ERBB1*) and *ALK*.[6,7]

More than half of HER2 mutations occur in the tyrosine kinase domain, with the majority located in exon 20.[2,8]



HER2 mutations have a similar prevalence to *ALK* and *ROS1*[2,7]



ALK=anaplastic lymphoma kinase; EGFR=epidermal growth factor receptor; FISH=fluorescence In situ hybridization; HER2=human epidermal growth factor receptor 2; KRAS=Kirsten rat sarcoma virus; NGS=next generation sequencing; NSCLC=non-small cell lung cancer; ROS1=ROS proto-oncogene 1, receptor tyrosine kinase; RT-PCR=reverse transcription-polymerase chain reaction.

Testing for mNSCLC mutations is a critical first step in diagnosing HER2 (*ERBB2*) mutations in mNSCLC[5]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend screening for HER2 (*ERBB2*) mutations in all patients with advanced or metastatic nonsquamous NSCLC, which includes adenocarcinoma mNSCLC[5]

NGS-based approaches are best able to detect the broad spectrum of HER2 mutations by utilizing tissue and liquid biopsies[5]

If a liquid biopsy result is negative, a tissue biopsy is recommended for confirmation[5]

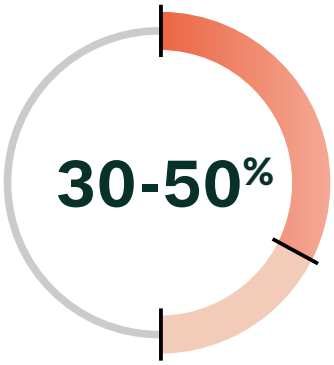
Patient selection for testing should not be based on smoking history, gender, or any other clinicopathologic features[5]

Review NGS results before initiating treatment

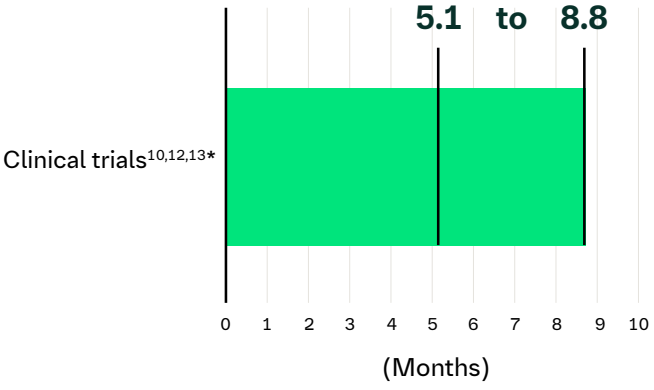
- Based on NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), most NGS panels effectively capture HER2 (*ERBB2*) mutation results.[5]
- Confirm biomarker results before initiating 1L treatment and reassess past results before initiating 2L treatment.[5]

Many patients with HER2 (*ERBB2*)-mutant mNSCLC did not respond to 1L treatment options[2,9]

ORR in patients using 1L chemotherapy-based treatment[10,11]



mPFS in patients using 1L chemotherapy-based treatment



*The population studied was diverse, with mutations extending beyond HER2 and including chemotherapy-based treatment with or without immunotherapy.[13]

1L=first-line; 2L=second-line; HER2=human epidermal growth factor receptor 2; mNSCLC=metastatic non-small cell lung cancer; mPFS=median progression-free survival; NCCN=National Comprehensive Cancer Network; NGS=next generation sequencing; ORR=objective response rate.

Updates are needed in the HER2 (*ERBB2*)-mutant mNSCLC treatment landscape

HER2 (*ERBB2*) is actionable in NSCLC

HER2 mutations have emerged as actionable drivers in NSCLC, with prevalence of 2-4%, similar to other drivers[1,2,5-7]

Review NGS results before initiating treatment

Based on NCCN Guidelines, most NGS panels effectively capture HER2 (*ERBB2*) mutation results[5]

Confirm results before initiating 1L treatment. Reassess past results at progression[5]

Significant unmet needs remain

Due to limited targeted treatment options across lines of therapy, patients with HER2 (*ERBB2*)-mutant mNSCLC have a poor prognosis compared with other driver mutations[2,9]

Boehringer Ingelheim Oncology is taking a diligent and broad approach in some of the most challenging, but potentially most impactful, areas of cancer research.

Learn more at **updateHER2.com**

1L=first line; HER2=human epidermal growth factor receptor 2; mNSCLC=metastatic non-small cell lung cancer; NCCN=National Comprehensive Cancer Network; NGS=next-generation sequencing; NSCLC=non-small cell lung cancer.

References: 1. Zhao J, Xia Y. *JCO Precis Oncol*. 2020;4:411-425. **2.** Yu X, Ji X, Su C. *Front Oncol*. 2022;12:860313. doi:10.2289/fonc.2022.860313 **3.** Loeffler E, Ancel J, Dalstein V, et al. *Life (Basel)*. 2023;14(1):64. **4.** Gaibar M, Beltrán L, Romero-Lorca A, et al. *J Oncol*. 2020;2020:6375956. **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN for Non-Small Cell Lung Cancer V.3.2025. © National Comprehensive Cancer Network, Inc. 2025). All right reserved. Accessed May 6, 2025. To view the most recent and complete version of the guidelines, 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. **6.** Riudavets M, Sullivan P, Planchard D. *ESMO Open*. 2021;6(5):100260. doi:10.1016/j.esmoop.2021.100260 **7.** Chevallier M, Borgeaud M, Addeo A, Friedlaender A. *World J Clin Oncol*. 2021;12(4):217-237. **8.** Robichaux JP, Elamin YY, Vijayan RSK, et al. *Cancer Cell*. 2019;36(4):444-457e7. doi:10.1016/j.ccell.2019.09.001 **9.** Uy NF, Merkhofer CM, Baik CS. *Cancers (Basel)*. 2022;14(17):4155. doi:10.3390/cancers14174155 **10.** Nützinger J, Lee JB, Low JL, et al. *Lung Cancer*. 2023;186:107385. doi:10.1016/j.lungcan.2024.107385 **11.** Brazel D, Kroening G, Nagasaka M. *BioDrugs*. 2022;36(6):717-729. **12.** Wang Y, Zhang S, Wu F, et al. *BMC Cancer*. 2018;18(1):326. doi:10.1186/s12885-018-4277-x **13.** Lin JJ, Chin E, Yeap BY, et al. *J Thorac Oncol*. 2019;14(1):135-140.

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