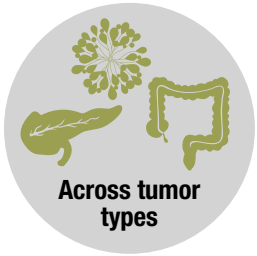
Pathogenic gene fusions are a contributing factor in 1 in 6 cancers[1]

Among 9624 patients who underwent tumor RNA sequencing, pathogenic gene fusions were found in 16.5% of samples[1]

Why should I be concerned about pathogenic gene fusions?

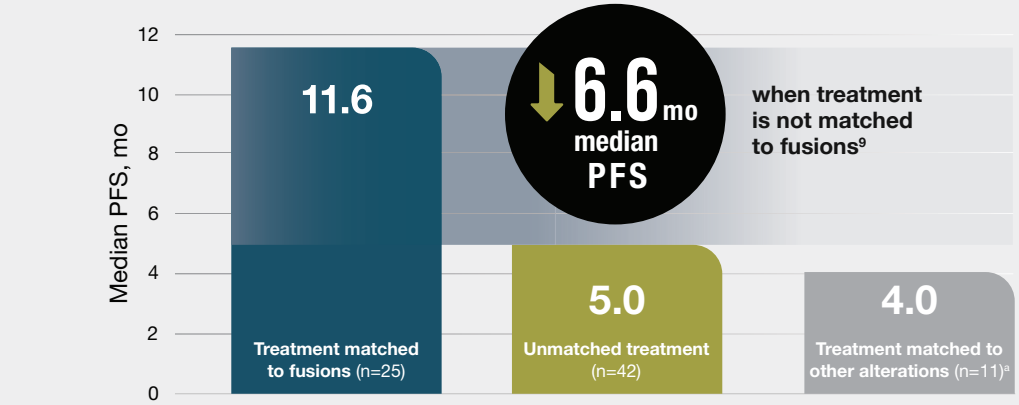
Gene fusions are independent prognostic factors for poor outcomes in lung cancer, regardless of age, sex, tumor tissue type, smoking status, and cancer stage (I-IV)[1-7]



They can occur across tumor types and play a critical role in oncogenesis[1-9]

How can targeting pathogenic gene fusions improve outcomes?

Pathogenic gene fusions may impact clinical management and outcomes, especially if targeted treatment is available.[1-7,9]



	Treatment matched to fusions (n=25)	Unmatched treatment (n=42)	Treatment matched to other alterations (n=11)[a]
Median PFS, mo (95% CI)	11.6 (4.0-35.4)	5.0 (3.3-8.8)	4.0 (3.3-NE)
PFS ≥6 mo	71.7%	44.6%	30.3%

In an analysis of 79 patients with identified gene fusions, poorer outcomes were observed in patients with pathogenic gene fusions who were not matched to fusion-targeted therapy.[9]

[a]Of the 12 patients who received treatment matched to other alterations, 1 had an unclear match and was excluded from pairwise comparison analysis.[9]

NE, not estimable; PFS, progression-free survival.

NRG1: A dangerous pathogenic gene fusion receiving increased attention

NRG1 fusions have been identified across many tumor types and generally occur in the absence of other driver mutations[2-8]

NRG1+ tumors are reported to be aggressive[2-7]

- 10x more likely to have concurrent intra- and extrathoracic metastases (50% *NRG1+* vs 5% *KRAS+*)[4]
- >2x more likely to have metastases at diagnosis (67% *NRG1+* vs 32% *KRAS+*)[4]
- *NRG1+* tumors are associated with lower OS, DFS, and PFS[4-7]

Studies observed histological features associated with increased tumor growth, invasiveness, recurrence, resistance to therapy, and metastasis in lung cancer.[2-7]

As with other genomic alterations, *NRG1* fusions are frequently associated with:

In a retrospective global registry study of 110 patients, *NRG1+* NSCLC was associated with limited response to available therapies[3]

Activity of systemic therapy in *NRG1+* NSCLC[3a]	ORR, %	Median PFS, mo (95% CI)
Platinum-doublet chemotherapy (n=15)	**13**	**5.8** (2.2-9.8)
Taxane-based chemotherapy (n=7)	**14**	**4.0** (0.8-5.3)
Combination chemotherapy and immunotherapy (n=9)	**0**	**3.3** (1.4-6.3)
Single-agent immunotherapy (n=5)	**20**	**3.6** (0.9-undefined)
Targeted therapy with kinase inhibitor (n=20)	**25**	**2.8** (1.9-4.3)

[a]Patients either diagnosed with or who developed metastatic disease during the course of their disease

How can you identify pathogenic gene fusions such as ***NRG1***?
Learn more at **FindTheFusions.com**

DFS, disease-free survival; *NRG1*, neuregulin 1; *NRG1+*, neuregulin 1 fusion positive; NSCLC, non–small cell lung cancer; ORR, overall response rate; OS, overall survival.

References: 1. Gao Q, Liang W-W, Foltz SM, et al. Driver fusions and their implications in the development and treatment of human cancers. *Cell Rep*. 2018;23(1):227-238.e3. doi:10.1016/j.celrep.2018.03.050 **2.** Dhanasekaran SM, Balbin OA, Chen G, et al. Transcriptome meta-analysis of lung cancer reveals recurrent aberrations in *NRG1* and Hippo pathway genes. *Nat Commun*. 2014;5:5893. doi:10.1038/ncomms6893 **3.** Drilon A, Duruisseaux M, Han J-Y, et al. Clinicopathologic features and response to therapy of *NRG1* fusion–driven lung cancers: the eNRGy1 Global Multicenter Registry. *J Clin Oncol*. 2021;39(25):2791-2802. doi:10.1200/JCO.20.03307 **4.** Chang JC, Offin M, Falcon C, et al. Comprehensive molecular and clinicopathologic analysis of 200 pulmonary invasive mucinous adenocarcinomas identifies distinct characteristics of molecular subtypes. *Clin Cancer Res*. 2021;27(14):4066-4076. doi:10.1158/1078-0432.CCR-21-0423 **5.** Shin DH, Lee D, Hong DW, et al. Oncogenic function and clinical implications of *SLC3A2-NRG1* fusion in invasive mucinous adenocarcinoma of the lung. *Oncotarget*. 2016;7(43):69450-69465. doi:10.18632/oncotarget.11913 **6.** Laskin J, Liu SV, Tolba K, et al. *NRG1* fusion-driven tumors: biology, detection, and the therapeutic role of afatinib and other ErbB-targeting agents. *Ann Oncol*. 2020;31(12):1693-1703. doi:10.1016/j.annonc.2020.08.2335 **7.** Rosas D, Raez LE, Russo A, Rolfo C. Neuregulin 1 gene (*NRG1*). A potentially new targetable alteration for the treatment of lung cancer. *Cancers (Basel)*. 2021;13(20):5038. doi:10.3390/cancers13205038 **8.** Liu SV. Plain language summary of *NRG1* fusions in cancer: current knowledge and treatment with afatinib and other drugs. *Future Oncol*. 2022;18(26):2865-2870. doi:10.2217/fon-2022-0073 **9.** Nikanjam M, Okamura R, Barkauskas DA, Kurzrock R. Targeting fusions for improved outcomes in oncology treatment. *Cancer*. 2020;126(6):1315-1321. doi:10.1002/cncr.32649 **10.** Jones MR, Williamson LM, Topham JT, et al. *NRG1* gene fusions are recurrent, clinically actionable gene rearrangements in *KRAS* wild-type pancreatic ductal adenocarcinoma. *Clin Cancer Res*. 2019;25(15):4674-4681. doi:10.1158/1078-0432.CCR-19-0191 **11.** Heining C, Horak P, Uhrig S, et al. *NRG1* fusions in *KRAS* wild-type pancreatic cancer. *Cancer Discov*. 2018;8(9):1087-1095. doi:10.1158/2159-8290.CD-18-0036

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