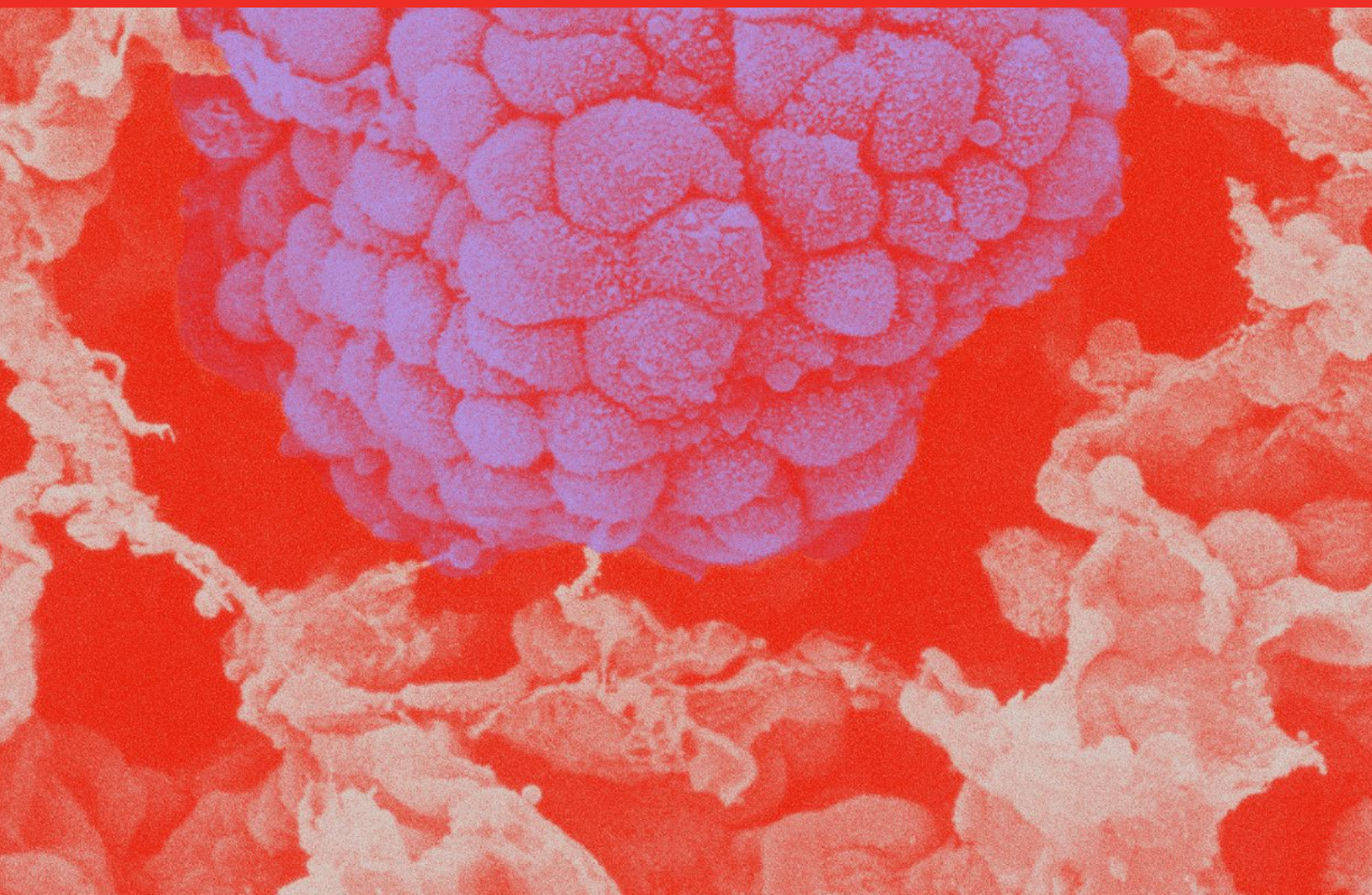
Lung Cancer Overview

J&J
Precision Medicine



A significant proportion of patients with advanced NSCLC do not receive biomarker-informed care[1,2]

Although there are a number of approved therapies for NSCLC patients with specific biomarkers:

~1/5 of patients

did not undergo biomarker testing[2*,†]

~20%

of patients did **not have any biomarker testing** ordered[2]

~1/3 of patients

received treatment before obtaining full biomarker test results[1‡]

27%

of patients with an actionable driver alteration were **treated with chemotherapy and/or ICI before test results were returned**[1]

~1/3 of patients

did not receive biomarker-matched treatment **even when an actionable biomarker has been identified**[2*,§]

29.2%

of patients received biomarker test results, but were **not treated with the appropriate, matched targeted therapy**[2]

*A study by the Personalized Medicine Coalition utilizing the Diaceutics proprietary DXRX Data Repository looked at the patient journey and evaluated the number and percentage of patients who advanced or were lost at each step within the clinical gap framework. The data were normalized to a patient population of 1000 to easily demonstrate the percentage of eligible patients who may be lost to receiving targeted therapies because of each clinical practice gap.[2]

†142 of 784 patients with advanced NSCLC.[2]

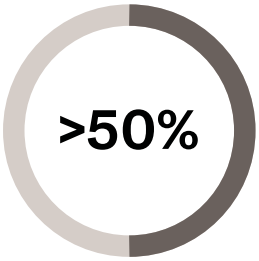
‡144 of 510 patients with stage IV NSCLC who tested positive for *EGFR, ALK, ROS1, BRAF, MET, RET, HER2*, and/or *NTRK1/2/3* in a real-world data study across multiple practices in the US.[1]

§147 of 503 patients with advanced NSCLC.[2]

Comprehensive testing is critical to ensure patients receive the most appropriate treatment[3]*

A majority of patients with mNSCLC have an actionable biomarker

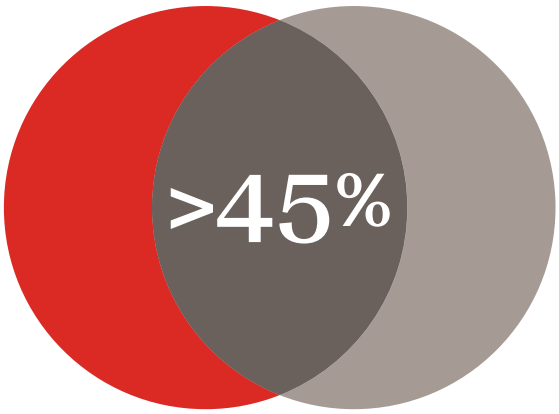
of patients with mNSCLC have an **actionable driver alteration**[4,5]



of patients with mNSCLC have an **actionable protein biomarker**[6–8]

Patients with driver alterations may also have protein overexpression

When certain driver alterations are present, **ICIs should not be used first-line** because targeted therapies yield higher response rates[3]*



of patients with NSCLC that are PD-L1+ also have an actionable driver alteration[9]

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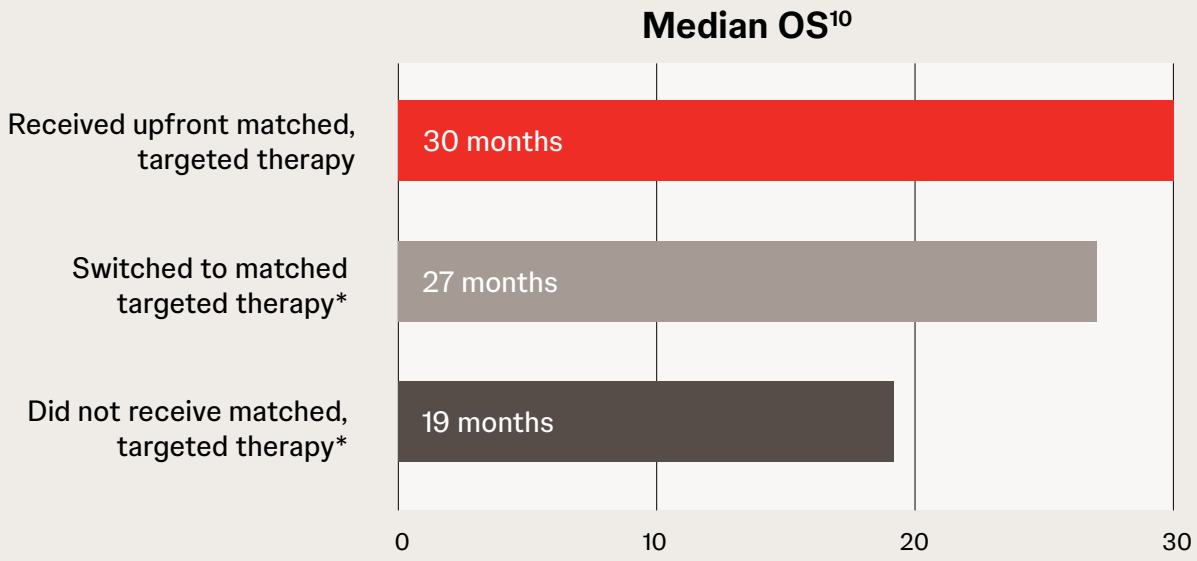
Impact on outcomes when matching 1L therapy to biomarker test results in NSCLC

Ensuring patients receive upfront biomarker-informed care impacts outcomes[10]

A retrospective study from January 1, 2015, to October 18, 2022, examined the impact of the timing and type of therapy given to 3540 patients with driver mutation-positive mNSCLC[10]



Switching to matched targeted therapy within **42 days or 2 treatment cycles** improved patient outcomes[10]

Opportunity to optimize

Wait for full biomarker testing results prior to initiating 1L therapy, if clinically feasible.[3†] Treatment can also be adjusted to align to biomarker testing results[11]

*Received chemotherapy, ICI, or both.[10]
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NGS is the optimal test that can detect multiple driver alterations simultaneously[12,13]

NGS interrogates a comprehensive panel of clinically relevant genetic biomarkers from patient samples[13,14]

In a single test, NGS can detect[3,15-19]*:

Multiple alterations of the same gene†

Driver Gene	Driver Alteration	Alteration Type
EGFR	Exon 19	Deletion
	Exon 20	Insertion‡
	Exon 21	SNV (L858R)

Multiple alteration types

SNV, CNV, indels, genomic rearrangements

Multiple driver alterations

ALK, BRAF, EGFR, HER2, KRAS, MET, NRG1, NTRK, RET, ROS1

Other valuable information[12]

Detection of resistance alterations that may impact treatment decisions[12]

Identification of new driver alterations to target after progression or prolonged stable disease on targeted therapies[12]

Testing for all actionable variants is important to help select the therapy indicated for a specific alteration[3]*

Opportunity to optimize

Identifying alterations via NGS can inform treatment decisions during the patient journey[12]

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†While these are common mutations, other less common mutations may be found.[19]
‡There may be >100 insertion options in EGFR exon 20.[19]

mNSCLC is defined by molecular drivers[4,5]

Frequency of oncogenic driver alterations in NSCLC (adenocarcinoma)[4]*

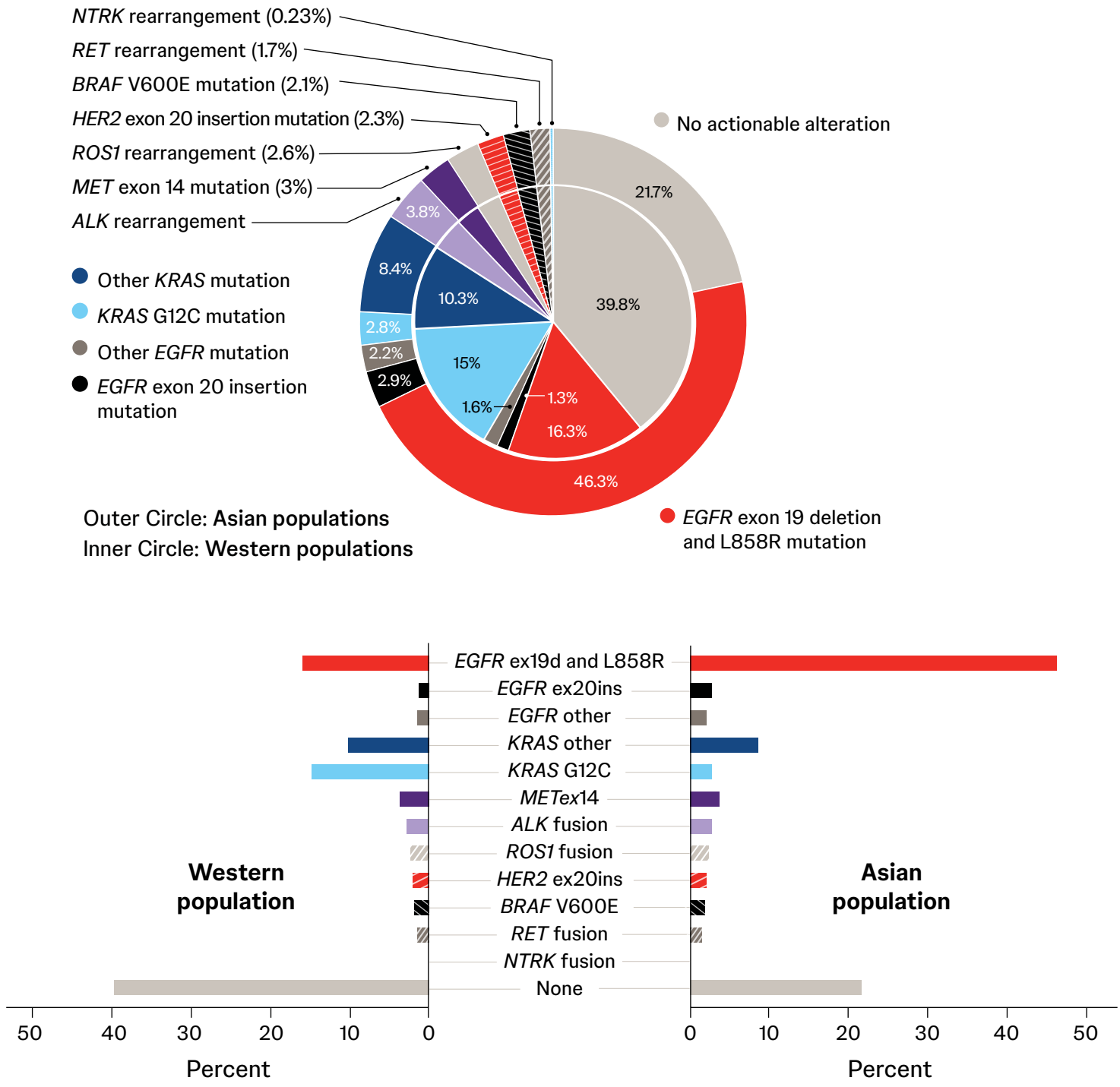
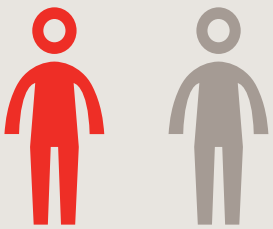


Image adapted from: Tan AC, Tan DSW. Targeted therapies for lung cancer patients with oncogenic driver molecular alterations. *J Clin Oncol.* 2022;40(6):611–625.

*Note: as of December 2024, *NRG1* is also an actionable driver alteration in mNSCLC.[3]

Many patients have actionable driver mutations[4,5]



>1 out of every 2

patients have 1 of the 10 currently actionable driver alterations[3-5]*

~1 out of every 5

patients has 1 of the 9 less common actionable driver alterations[4,5,20]†

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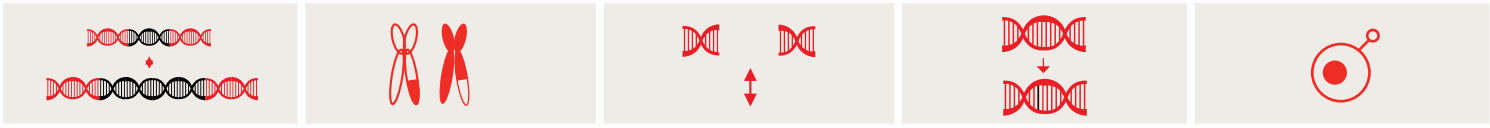
†Less common driver alterations refers to drivers with a prevalence of less than 5%.

Complete biomarker testing requires testing for different biomarker types

Driver alterations: Can be the result of a number of different types of genetic alterations[12,21]

Protein biomarker



CNV[12]	Fusion/ rearrangement[12]	INDEL[12]	SNV[12]	
A deletion or insertion of a larger segment of DNA[12]	A chromosome breaks and the fragmented pieces re-attach to different chromosomes[12]	Addition or deletion of ≥1 nucleotides into a segment of DNA[12]	Substitution of 1 nucleotide for another[12]	A protein found on cells in tissue or bodily fluids[21]
MET amplifications are an emerging biomarker in NSCLC[12,15]	*ALK, NTRK, RET, ROS1*[12,15]	*EGFR, HER2, MET*ex14[12,15]	*BRAF, EGFR, HER2, KRAS*[12,15]	PD-L1[15]
	Actionable biomarkers in mNSCLC[12,15]			

Testing capabilities differ by methodology

Oncogenes can have multiple actionable driver alterations or alteration types

For example:

Driver gene	Driver alteration	Alteration type
EGFR[19]	Exon 19	Deletion
	Exon 20	Insertion*
	Exon 21	SNV (L858R)
MET[22]	*MET*ex14	2- to 193-bp deletion, SNV
RET[23]	*RET* fusion	Wide range of fusions†

Options for detecting these alterations include

PCR	NGS
Tests for individual, known alterations[13,24]	**Sequences DNA samples and identifies alteration by comparing with a normal/control sample[13,14]**

There are many sequence options for insertions, deletions (if more than a point deletion), and fusions. **NGS is the optimal test that can detect multiple driver alterations simultaneously[13]**

*There may be >100 insertion options in *EGFR* exon 20.[19]
†In a recent study, 61 novel *RET* fusions were identified across solid tumor types.[23]

Guideline recommendations for testing 13 actionable biomarkers in NSCLC

Biomarker	National Comprehensive Cancer Network® (NCCN®)[3]*	CAP/IASLC/AMP[25,26]	ASCO[27]	Testing technology[3,15,20]
ALK	●	●	●	NGS, FISH (historical standard), IHC (validated against FISH)
BRAF	●	●	●	Any appropriate, validated technology, subject to external quality assurance
EGFR	●	●	●	Any appropriate, validated technology, subject to external quality assurance
ERBB2 (HER2)	●	●	●	NGS
HER2†	●	○	○	IHC
KRAS	●	●	●	NGS, RT-PCR, pyrosequencing
HGFR(*MET*)†	●	○	○	IHC
MET	●	●	●	NGS, IHC, FISH
NRG1	●	○	○	NGS
NTRK1/2/3	●	○	○	NGS, IHC, FISH, RT-PCR
PD-L1	●	●	●	IHC
RET	●	●	●	NGS, FISH, RT-PCR
ROS1	●	●	●	NGS, FISH (trial-validated standard), IHC to select for confirmatory FISH

● Testing recommended ● Expanded panel testing recommended ○ No guideline recommendations to date

Guidelines from multiple US organizations recommend testing for all actionable biomarkers in mNSCLC, often via expanded panel testing[3,25-27]*

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†During initial evaluation, the priority should be PD-L1 testing and multigene panel testing; if tissue allows, additional testing can be performed (eg, HER2 IHC or HGFR *[MET]* IHC).[3]

Biomarkers are integral to the treatment of NSCLC[1,3,10,25,27]

Patient outcomes are linked to comprehensive biomarker testing for targeted therapies[1,10]

Guideline-recommended treatment for lung cancer is comprehensive broad-based testing[3,25,27]*

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1L, first-line; *ALK*, anaplastic lymphoma kinase; AMP, Association for Molecular Pathology; ASCO, American Society of Clinical Oncology; *BRAF*, B-Raf proto-oncogene, serine/threonine kinase; CAP, College of American Pathologists; CNV, copy number variant; DNA, deoxyribonucleic acid; *EGFR*, epidermal growth factor receptor; ERBB2, erb-b2 receptor tyrosine kinase 2; FDA, U.S. Food and Drug Administration; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; HGFR(*MET*), hepatocyte growth factor receptor (mesenchymal-epithelial transition) also known as cMet; IASLC, International Association for the Study of Lung Cancer; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; INDEL, insertion or deletion; *KRAS*, Kristen rat sarcoma virus; *MET*, mesenchymal epithelial transition; mNSCLC, metastatic non-small cell lung cancer; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; *NRG1,* neuregulin 1; NSCLC, non-small cell lung cancer; *NTRK*, neurotrophic tyrosine receptor kinase; OS, overall survival; PCR, polymerase chain reaction; PD-L1, programmed death-ligand 1; *RET*, receptor tyrosine kinase; *ROS1*, ROS proto-oncogene 1, receptor tyrosine kinase; RT-PCR, reverse transcription polymerase chain reaction; SNV, single-nucleotide variant; US, United States.

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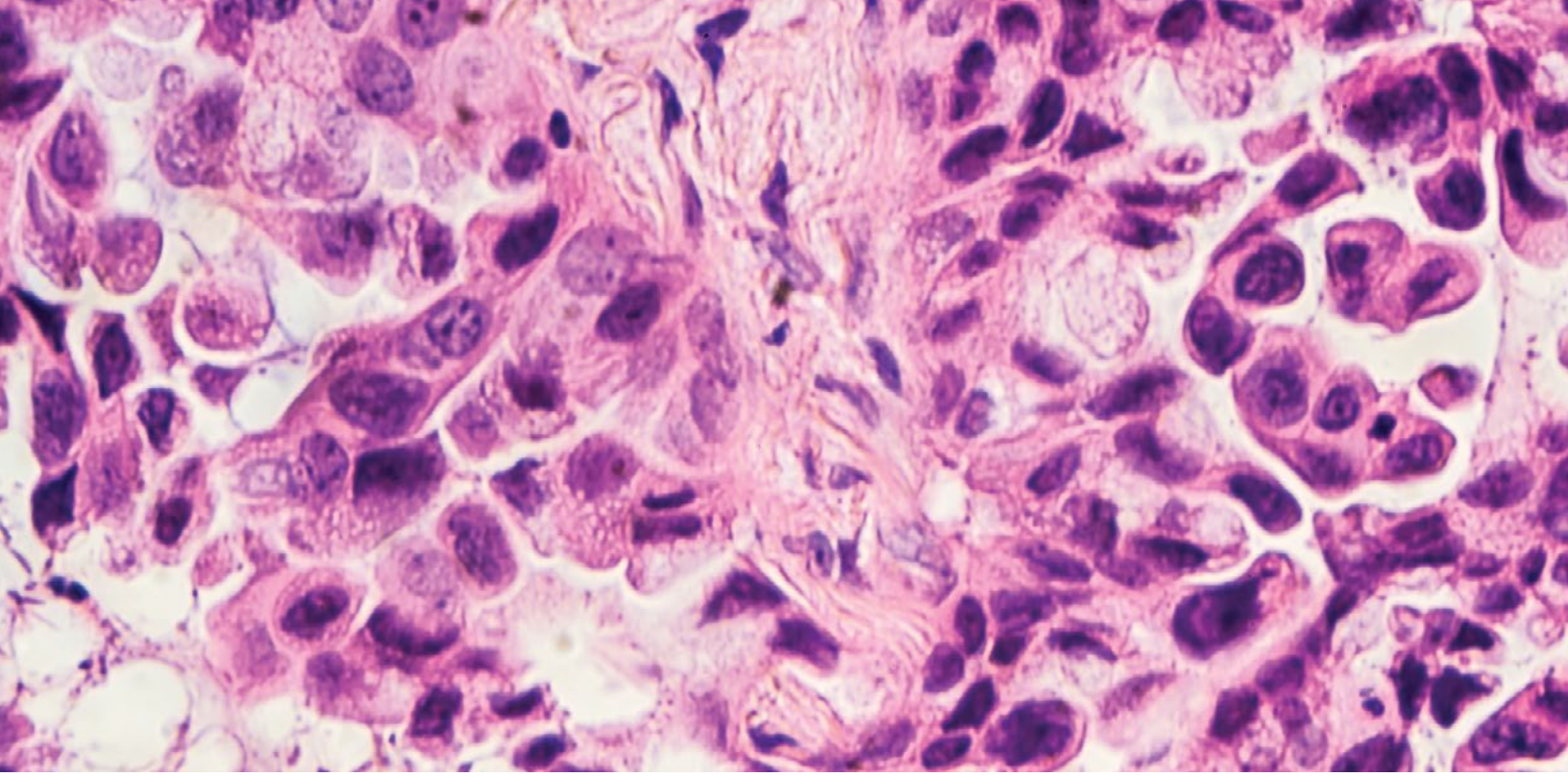

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