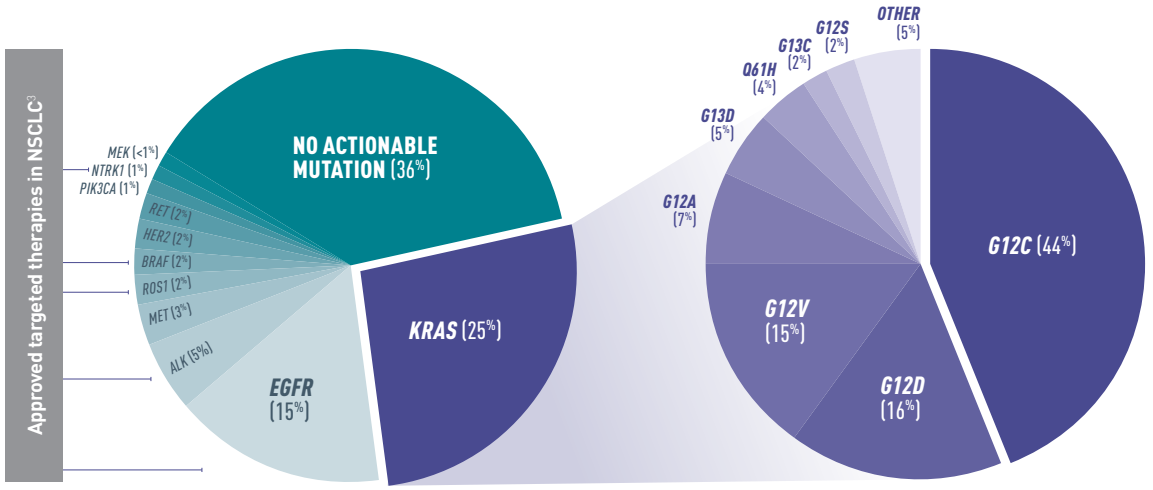
KRAS IS THE MOST COMMON DRIVER MUTATION IN NSCLC

KRAS G12C is a key oncogenic mutation in NSCLC[1,2]

KRAS Is the Most Common Driver Mutation in NSCLC[2]

KRAS G12C Represents Nearly Half (44%) of All *KRAS* Mutations in NSCLC[1]



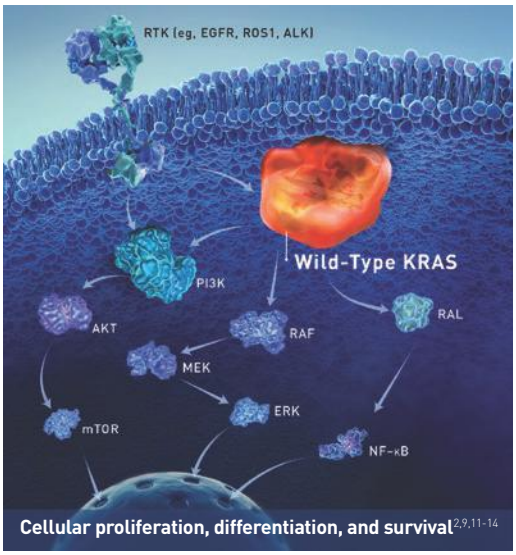
13% (~1 in 8) of patients in the US with NSCLC have the *KRAS G12C* driver mutation[4]

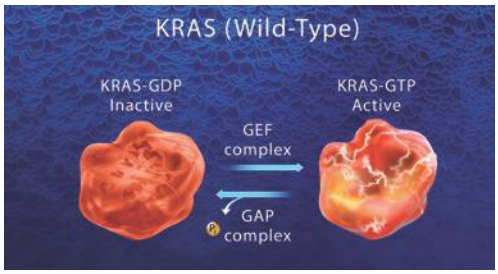
~23,000 new patients are diagnosed with *KRAS G12C* mutated lung cancer annually in the US[5]

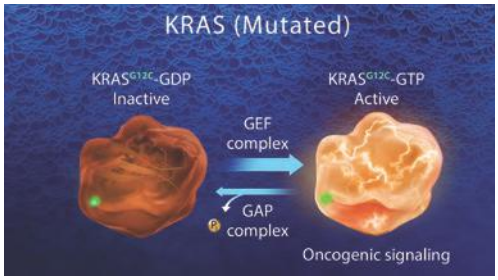
Targeted therapy is not currently available for patients with *KRAS* mutations[6]

KRAS mutations are prognostic for poor survival in patients with NSCLC[7,8,*]

KRAS^{G12C} mutant protein promotes oncogenic signaling, supporting cancer cell growth and survival[9,10]







KRAS cycles between inactive (GDP-bound) and active (GTP-bound) states, serving as an on/off molecular switch to regulate downstream signaling pathways[9,14]

The *KRAS G12C* mutation favors the active form of the KRAS mutant protein, supporting cancer cell growth and survival[9-11]

Amgen is committed to investigating KRAS^{G12C} as a potential approach in NSCLC

*Based on two retrospective studies, the first study analyzed outcomes for 179 patients with surgically resected NSCLC from the University of Michigan Health System between 1991 and 2007.[7] The second study analyzed outcomes for 129 patients with advanced NSCLC treated with chemotherapy at the Department of Pneumology University Hospital Pilsen between 2006 and 2015.[8]

AKT, protein kinase B; ALK, anaplastic lymphoma kinase; BRAF, proto-oncogene B-Raf; EGFR, epidermal growth factor receptor; ERK, extracellular signal-regulated kinase; GAP, GTPase-activating protein; GDP, guanosine diphosphate; GEF, guanine nucleotide exchange factor; GTP, guanosine triphosphate; HER2, human epidermal growth factor receptor 2; KRAS, Kirsten rat sarcoma; MEK, mitogen-activated protein kinase kinase; MET, mesenchymal-to-epithelial transition; mTOR, mammalian target of rapamycin; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; NSCLC, non-small cell lung cancer; NTRK1, neurotrophic tyrosine receptor kinase 1; Pi, inorganic phosphate; PI3K, phosphoinositide 3-kinase; PIK3CA, phosphoinositide 3-kinase, catalytic, alpha polypeptide; RAF, rapidly accelerated fibrosarcoma; RAL, Ras-like; RET, rearranged during transfection; ROS1, c-ros oncogene 1; RTK, receptor tyrosine kinase.

Biomarker testing is critical for identifying driver mutations in NSCLC

Identification of driver mutations may allow for targeted therapeutic interventions that lead to improved patient outcomes[15,16]

Guideline Recommendations for Biomarker Testing

PREDICTIVE BIOMARKERS	NCCN Guidelines®†,†	CAP/IASLC/AMP Guidelines[17]	ASCO Guidelines[18,19]
EGFR	●	●	●
ALK	●	●	●
ROS1	●	●	●
BRAF	●	●	●
PD-L1	●	●	●
NTRK	●	●	●

PROGNOSTIC/EMERGING BIOMARKERS	NCCN Guidelines®†,†	CAP/IASLC/AMP Guidelines[17]	ASCO Guidelines[19]
KRAS	●	●	●
MET	●	●	●
RET	●	●	●
HER2	●	●	●
TMB	●	●	●

● Testing recommended
● Expanded panel testing recommended
● Single-gene or expanded panel testing recommended
● Single-gene or expanded panel testing may be useful
● No guideline recommendations to date

†NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

Despite guideline recommendations, many patients do not receive testing for biomarkers or appropriate targeted therapy[20-22]
Are you testing for biomarkers in your patients with NSCLC?

Considerations for sample collection and selection of testing platform

Sample Collection

	Tissue Biopsy	Liquid Biopsy
METHOD	Gold standard; tissue extracted from primary tumor[23,24]	Blood sample containing cell-free DNA[23,24]
TUMOR HETEROGENEITY	Limited to composition of tumor biopsies[23,24]	Captures tumor heterogeneity from primary tumors and metastases[23,24]
SAMPLE COLLECTION	Invasive with possible complications[23]	Minimally invasive blood sample allows monitoring throughout disease[23,24]
SAMPLE REQUIREMENTS	Sufficient tissue should be collected at diagnosis to optimize molecular testing[4]	Consider when insufficient tissue available or patient is unfit for invasive biopsy[25]
SAMPLE INTEGRITY	DNA/RNA structural changes possible in FFPE samples[23]	Collection method may require fast turnaround time to ensure sample integrity[25]

Single-Gene vs Multigene Platforms

	Single Gene (eg, PCR)	Multigene (eg, NGS)
METHOD	Detects prespecified mutations[25]	Detects multiple biomarkers[29]
GENES ASSESSED	A single gene of interest[25]	Multiple genes in targeted panels[29]
TURNAROUND TIME	1–7 days[26,27]	7–20 days[26]
COST	Lower[28]	Higher[28]

Liquid biopsy may be used when insufficient tissue is available or when the patient is not medically fit for invasive tissue sampling[25]

KRAS testing can be performed as part of a multigene panel or as a single-gene test[17,19]

Learn more at FindKRASG12C.com

AMP, Association for Molecular Pathology; ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; FFPE, formalin-fixed paraffin-embedded; IASLC, International Association for the Study of Lung Cancer; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; NTRK, neurotrophic tyrosine receptor kinase; PCR, polymerase chain reaction; PD-L1, programmed cell death ligand 1; TMB, tumor mutational burden.

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