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

**KRAS G12C** is a key oncogenic mutation in NSCLC1,2

**KRAS G12C** mutant protein promotes oncogenic signaling, supporting cancer cell growth and survival9,10

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

KRAS cycles between inactive (GDP-bound) and active (GTP-bound) states, serving as an on/off molecular switch to regulate downstream signaling pathways.7,14

The KRAS G12C mutation favors the active form of the KRAS mutant protein, supporting cancer cell growth and survival.11

Approved targeted therapies in NSCLC

Targeted therapy is not currently available for patients with KRAS mutations1

KRAS mutations are prognostic for poor survival in patients with NSCLC.7,8

~23,000 new patients are diagnosed with KRAS G12C mutated lung cancer annually in the US5

13% (~1 in 8) of patients in the US with NSCLC have the KRAS G12C driver mutation4

**KRAS G12C** represents nearly half (44%) of all KRAS mutations in NSCLC1

**KRAS** is the most common driver mutation in NSCLC2

**KRAS G12C** is a key oncogenic mutation in NSCLC1,2

**KRAS** is the most common driver mutation in NSCLC3

**KRAS (Wild-Type)**

**KRAS-GDP Inactive**

GAP complex

**GAP complex**

**KRAS-GTP Active**

Cellular proliferation, differentiation, and survival2,9-14

Cellular proliferation, differentiation, and survival2,9-14

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; 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; 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 outcomes15,16

Guideline Recommendations for Biomarker Testing

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*NCN Clinical Practice Guidelines in Oncology (NCN Guidelines)*

Despite guideline recommendations, many patients do not receive testing for biomarkers or appropriate targeted therapy26-22

Are you testing for biomarkers in your patients with NSCLC?

Considerations for sample collection and selection of testing platform

**Sample Collection**

- **Tissue Biopsy**
  - Gold standard; tissue extracted from primary tumor23-25
  - Limited to composition of tumor biopsies23-25
  - Invasive with possible complications25
  - Insufficient tumor tissue in some samples23-25
  - Sample processing may result in reduced quality of results23-25

- **Liquid Biopsy**
  - Blood sample containing cell-free DNA21,23
  - Captures tumor heterogeneity from primary tumors and metastases23-25
  - Minimally invasive blood sample allows monitoring throughout disease23,25
  - Not all tumors shed sufficient DNA for detection25
  - Collection method may require faster processing to ensure sample integrity25

Liquid biopsy may be used when insufficient tissue is available or when the patient is not medically fit for invasive tissue sampling25

**Single-Gene vs Multigene Platforms**

- Single Gene (eg, PCR)
  - Detects prespecified mutations23-25
  - A single gene of interest25
  - 1-7 days26,27

- Multigene (eg, NGS)
  - Detects multiple biomarkers23-25
  - Multiple genes in targeted panels25
  - 7-20 days23
  - Higher29

KRAS testing can be performed as part of a multigene panel or as a single-gene test17,19

Learn more at FindKRASG12C.com

References:
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