

# Adagrasib

- Combination therapy of adagrasib and abemaciclib in non-small cell lung cancer brain metastasis models genomically characterized by KRAS-G12C and homozygous loss of CDKN2A
- Hydroxychloroquine prevents resistance and potentiates the antitumor effect of SHP2 inhibition in NF1-associated malignant peripheral nerve sheath tumors
- A real-world pharmacovigilance study of KRAS G12C mutation inhibitors based on the food and drug administration adverse event reporting system

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**Adagrasib** (brand name **Krazati**) is an oral, small-molecule inhibitor that **specifically targets KRAS G12C mutations**, which are commonly found in certain cancers, including:

\* **Non-small cell lung cancer (NSCLC)**

\* **Colorectal cancer**

\* **Pancreatic cancer**

## Key Points

\* **Mechanism of action:**

Adagrasib irreversibly binds to the **KRAS G12C mutant protein**, locking it in its inactive state. This prevents the downstream signaling that promotes tumor growth.

\* **Approved indication:**

As of late 2022, the FDA approved adagrasib for **NSCLC with KRAS G12C mutations** in patients who have received at least one prior systemic therapy.

\* **Combination therapy potential:**

Adagrasib is being studied in **combination with other agents**, such as:

- **Immune checkpoint inhibitors** (e.g., pembrolizumab)
- **EGFR inhibitors** in colorectal cancer (e.g., cetuximab)
- **SHR inhibitors or MEK inhibitors** in preclinical models

Advantages over sotorasib (another KRAS G12C inhibitor):

Some studies suggest adagrasib may have better **central nervous system penetration**, offering hope for patients with brain metastases.

## [Adagrasib for Non-small cell lung cancer intracranial metastases](#)

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