Promising KRAS Drugs

Sotorasib and adagrasib target a specific cancer-causing mutation found in those with non-small-cell lung cancer and colorectal cancer.

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After three decades of unsuccessful attempts, researchers are finally cracking the KRAS code, with two experimental KRAS inhibitors moving into late-stage clinical trials.

The KRAS gene makes proteins involved in signaling pathways that regulate cell growth; mutations allow cancer cells to grow out of control. Once considered “undruggable,” KRAS is the most commonly altered gene in people with cancer.

Sotorasib (formerly AMG 510) targets a specific mutation, known as KRAS G12C, found in about 14% of non-small-cell lung cancer (NSCLC) and a smaller proportion of other solid tumors.

In the Phase I/II CodeBreaK 100 study, sotorasib led to tumor shrinkage in 32% of patients with advanced NSCLC. Another 56% had stable disease, for a combined disease control rate of 88%. Among people with colorectal cancer, 7% were responders, and 67% had stable disease, for a disease control rate of 74%. Four of the 28 people with other types of cancer (14%) had a partial response, and the disease control rate was 75%.

Adagrasib (formerly MRTX849), which targets the same mutation, likewise demonstrated good results in the Phase I/II KRYSTAL-1 trial. In an analysis of 51 people with advanced NSCLC, 45% had a partial response, and all but two of the rest had stable disease, for a disease control rate of 96%. Of the 18 treated patients with colorectal cancer, three (17%) had a partial response, and the disease control rate was 94%. Among the six people with other advanced solid tumors, four had partial remission, and two had stable disease.

“It’s an inspiring and exciting time in the oncology field to see potential targeted therapeutic options for patients with the KRAS G12C mutation, a patient population that has historically faced limited treatment options,” says KRYSTAL-1 investigator Pasi Jänne, MD, PhD, of Dana-Farber Cancer Institute in Boston.
