

Trial finds that adagrasib demonstrates durable clinical activity in patients with KRAS-G12C mutations

September 9 2023



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The oral, selective KRAS G12C inhibitor KRAS-G12C inhibitor adagrasib demonstrated durable clinical activity, with a median overall survival of 14.1 months and approximately one in three patients alive at two years, according to research presented today at the International Association for the Study of Lung Cancer (IASLC) 2023 World [Conference](#) on Lung Cancer in Singapore.

KRAS-G12C mutations occur in approximately 14% of patients with NSCLC. The KRYSTAL-1 study, a multi-cohort Phase 1/2 trial, evaluated adagrasib as a monotherapy or in combination for patients with KRAS-G12C-mutated solid tumors. The U.S. Food and Drug Administration (FDA) already granted accelerated approval of adagrasib for patients with previously treated KRAS-G12C-mutated advanced/metastatic NSCLC based on data from this study. Additionally, the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) are currently reviewing the drug.

In the two-year follow-up, pooled analysis of the Phase 1/1b Cohort and Phase 2 Cohort A, 132 patients with KRAS-G12C-mutated NSCLC were treated with adagrasib 600 mg orally twice daily. The median age of patients was 64 years, with 56.8% being female. At baseline, 19.7% of patients had central nervous system metastases. Patients had received a median of two prior therapies, including platinum-based and checkpoint inhibitor therapies.

According to Shirish Gadgeel, MD from Henry Ford Cancer Institute,

Henry Ford Health System, in Detroit, Mich., the results showed a favorable objective response rate (ORR) of 43.0%, with a median duration of response (DOR) of 12.4 months. The [median progression-free survival](#) (PFS) was 6.9 months, and the [median overall survival](#) (OS) was 14.1 months. Notably, 52.8% of patients were still alive at one year, and approximately one in three patients (31.3%) remained alive at two years. The findings suggest durable clinical activity of adagrasib for KRAS-G12C-mutated NSCLC.

"The study data demonstrates promising results, providing hope for patients with this specific mutation," Dr. Gadgeel said. "Exploratory analyses indicated that the presence of co-mutations, such as KEAP1, STK11, or TP53, may impact the clinical benefit of adagrasib and warrant further investigation."

Dr. Gadgeel reported that treatment-related adverse events were manageable, with grade ≥ 3 TRAEs occurring in 40.9% of patients. Only 2.3% of patients experienced grade 5 TRAEs, including pneumonitis, cardiac failure, and pulmonary hemorrhage.

The ongoing Phase 3 trial evaluating adagrasib monotherapy compared with docetaxel in previously treated advanced KRAS-G12C-mutated NSCLC holds great promise and could further establish adagrasib as an essential treatment option for [patients](#) with this specific mutation, he reported.

Provided by International Association for the Study of Lung Cancer

Citation: Trial finds that adagrasib demonstrates durable clinical activity in patients with KRAS-G12C mutations (2023, September 9) retrieved 28 April 2024 from <https://medicalxpress.com/news/2023-09-trial-adagrasib-durable-clinical-patients.html>

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