FDA Approves Targeted Therapy for Lung Cancer With EGFR Mutations

Rybrevant is the first treatment for people with advanced non-small-cell lung cancer whose tumors have EGFR exon 20 insertion mutations.

May 25, 2021 By Liz Highleyman

On May 21, the Food and Drug Administration (FDA) granted accelerated approval of Rybrevant (amivantamab), a new targeted therapy for people with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumors have specific genetic alterations known as epidermal growth factor receptor (EGFR) exon 20 insertion mutations.

"Today's FDA approval is an important development for people living with non-small-cell lung cancer with exon 20 insertion mutations who, until now, have had no approved treatment options to target their disease," Jill Feldman, cofounder of the patient advocacy group EGFR Resisters, said in a Janssen press release. "We are excited by the promise this new treatment option brings to people with this particular type of lung cancer and their families."

Lung cancer is the leading cause of cancer-related death in the United States and worldwide; NSCLC accounts for more than 80% of all lung cancer cases, according to the American Cancer Society.

Targeted therapies work against cancer with specific genetic mutations or other distinct characteristics. NSCLC tumors can have several targets—including EGFR, ALK, MET and ROS1—that make them susceptible to such drugs. EGFR is a protein that plays a role in cell growth and blood vessel development. Although there are several approved oral tyrosine kinase inhibitors targeting EGFR, they generally don't work well for NSCLC driven by EGFR exon 20 insertion mutations. Some 2% to 3% of people with NSCLC have these mutations, which are associated with poorer prognosis.

Rybrevant, from Janssen, is a bispecific monoclonal antibody that targets both EGFR and MET receptors. It is approved for adults who have lung tumors with EGFR exon 20 insertion mutations and whose disease has progressed on or after platinum-based chemotherapy. The FDA also approved a companion diagnostic test (Guardant360 CDx) that detects whether the mutation is present.

"Advances in precision oncology continue to facilitate drug development, allowing diseases like

lung cancer to be subset into biomarker-defined populations appropriate for targeted therapies," Julia Beaver, MD, of the FDA's Oncology Center of Excellence said in a press release. "With today's approval, for the first time, patients with NSCLC with EGFR exon 20 insertion mutations will have a targeted treatment option."

The approval was based on results from the Phase I CHRYSALIS trial (NCT02609776), which evaluated Rybrevant both as monotherapy and in combination with the experimental tyrosine kinase inhibitor lazertinib.

The monotherapy analysis included 81 NSCLC patients with EGFR exon 20 insertion mutations who progressed despite platinum chemotherapy. They received IV infusions of Rybrevant once weekly for four weeks, then every two weeks thereafter until they experienced disease progression or unacceptable side effects.

The overall response rate, meaning complete or partial tumor shrinkage, was 40%, including 4% with complete remission. The median duration of response was 11.1 months, and 63% of patients had a response lasting six months or longer. The study results were presented at last year's American Society of Clinical Oncology annual meeting and at the 2020 World Lung Cancer Conference.

In the CHRYSALIS study, 11% of participants permanently stopped treatment due to adverse events, but three quarters interrupted treatment temporarily. According to the Rybrevant package insert, the most common adverse reactions are infusion reactions, skin rash, nail infections, mouth sores, fatigue, pain, nausea, vomiting, constipation, shortness of breath, cough and swelling. The insert includes warnings about severe infusion reactions, interstitial lung disease, severe skin problems and eye problems. People taking the drug should avoid sun exposure.

Therapies that receive FDA accelerated approval based on overall response rate are expected to undergo further testing in larger trials to confirm clinical benefits, and the agency can rescind approval if they do not measure up. Rybrevant is currently being evaluated in the Phase III MARIPOSA trial (NCT04487080) in combination with lazertinib and in the Phase III PAPILLON trial (NCT04538664) in combination with carboplatin and pemetrexed chemotherapy.

Janssen's CarePath provides patient support, resources and help obtaining and paying for Rybrevant. "Janssen will work closely with payers and providers to ensure Rybrevant is broadly accessible and affordable for people with NSCLC with EGFR exon 20 insertion mutations," the company states. Visit JanssenCarePath.com/Rybrevant or call 1-833-792-7382.

Click here for full prescribing information for Rybrevant.

Click here to learn more about lung cancer.

© 2026 Smart + Strong All Rights Reserved.