FDA Approves New Treatment for Chronic Lymphocytic Leukemia

Calquence is the second therapy approved under a new program that lets companies simultaneously apply for approval in multiple countries.

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On November 21, the Food and Drug Administration (FDA) approved Calquence (acalabrutinib) for the treatment of adults with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). The medication may be used as initial therapy for people starting treatment for the first time or as a subsequent therapy for those who have tried previous medications.

The targeted therapy, from AstraZeneca, was simultaneously approved in Australia and Canada under a new program called Project Orbis that enables concurrent submission and review of experimental cancer therapies in multiple countries.

Calquence inhibits Bruton's tyrosine kinase (BTK), which plays a role in maturation of B cell, which grow out of control or do not function normally in people with leukemia and lymphoma. It was first approved in 2017 for people with mantle cell lymphoma. Calquence is taken as a capsule twice daily, with or without food.

CLL, the most common type of leukemia in adults, involves overproduction of abnormal white blood cells—usually antibody-producing B cells—in the blood and bone marrow. Although traditional chemotherapy can sometimes put CLL into remission, relapse is common. SLL is a slow-growing type of lymphoma in which immature white blood cells build up in lymph nodes.

Approval was based on two clinical trials that compared Calquence against standard treatments. Findings will be presented at the American Society of Hematology annual meeting next month, according to AstraZeneca.

The Phase III ELEVATE-TN study included 535 participants with previously untreated CLL. They were randomly assigned to receive Calquence alone (known as monotherapy), Calquence plus the CD20 antibody Gazyva (obinutuzumab) or Gazyva plus the chemotherapy drug chlorambucil.

After more than two years of follow-up, those who received Calquence alone or in combination had longer progression-free survival (PFS), meaning they were still alive and their cancer had not worsened. The median PFS was 22.6 months in the Gazyva plus chlorambucil group but was not reached in either the Calquence monotherapy or Calquence combination groups because most

participants were still responding. Overall response rates, meaning complete or partial remission, were 94% for Calquence plus Gazyva, 86% for Calquence alone and 79% for Gazyva plus chlorambucil. [Editor's note: see the ASH abstract here.]

The ASCEND trial enrolled 310 people with previously treated relapsed or refractory (nonresponsive) CLL. They were randomized to receive Calquence alone or their doctor's choice of either Zydelig (idelalisib) plus rituxumab (Rituxan or a biosimilar product) or rituxumab plus the chemotherapy drug bendamustine.

After a median 16.1 months of follow-up, progression-free survival was again significantly longer in the Calquence group (median not reached) compared with the standard therapy group (median 16.5 months). After a year, 88% of Calquence recipients had not experienced disease progression compared with 68% of standard therapy recipients—a 69% reduction in the risk of disease progression or death.

Calquence is generally safe and well tolerated. Common side effects include headache, diarrhea and muscle pain. Calquence can cause a decrease in red blood cells (anemia), which can lead to fatigue, white blood cells (neutropenia), which can lead to infections, and platelets (thrombocytopenia), which can lead to easy bleeding.

Less common but more serious adverse events may include severe blood cell depletion, heavy bleeding, opportunistic infections, heart rhythm abnormalities and an increased risk of developing other cancers. The FDA advises that people taking Calquence should use sun protection because of the increased risk of skin cancer. Women who are pregnant or breastfeeding should not use Calquence.

"Tolerability remains an issue in the current treatment landscape of chronic lymphocytic leukemia, which may require ongoing therapy for many years," Jeff Sharman, MD, of Willamette Valley Cancer Institute, said in an AstraZeneca press release. "In the ELEVATE-TN and ASCEND trials comparing Calquence to commonly used treatment regimens, Calquence demonstrated a clinically meaningful improvement in progression-free survival in patients across multiple settings, while maintaining its favorable tolerability and safety profile."

Click here to read an FDA news release about the approval.

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