RNS Number : 7829T
AstraZeneca PLC
20 February 2026

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Calquence plus venetoclax approved in the US as first all-oral, fixed-duration combination for patients with chronic lymphocytic leukaemia in the 1st-line setting

Calquence plus venetoclax demonstrated statistically significant and clinically meaningful improvement in progression-free survival vs. chemoimmunotherapy, with 77% of patients progression free at three years in AMPLIFY Phase III trial

AstraZeneca's *Calquence* (acalabrutinib) in combination with venetoclax has been approved in the US as the first all-oral, fixed-duration regimen for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL).

The approval by the US Food and Drug Administration (FDA) was based on positive results from the AMPLIFY Phase III trial, which were presented at the American Society of Hematology 2024 Annual Meeting and published in *The New England Journal of Medicine*.[1,2]

CLL is the most common type of leukaemia in adults.[3] An estimated 18,500 people were treated for CLL in the 1st-line setting in the US in 2024.[4]

Jennifer Brown, MD, PhD, Director of the CLL Center of the Division of Hematologic Malignancies, Dana-Farber Cancer Institute, and the Worthington and Margaret Collette Professor of Medicine at Harvard Medical School, and principal investigator of the AMPLIFY trial, said: "The continuous regimens frequently used to treat chronic lymphocytic leukaemia often come with side effects that may become burdensome to patients over time. The US approval of the *Calquence* combination offers patients an all-oral, 14-month, fixed-duration treatment option that is highly effective and well-tolerated, and gives physicians greater flexibility to tailor treatment plans for individual patient needs and goals."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "Today's approval delivers the first all-oral, fixed-duration BTK inhibitor-based regimen in the US for the treatment of chronic lymphocytic leukaemia. This *Calquence* combination has the potential to meaningfully change 1st-line chronic lymphocytic leukaemia treatment decisions and underscores our commitment to improving on the current standard of care for people living with blood cancers."

Gwen Nichols, MD, Chief Medical Officer of Blood Cancer United, formerly The Leukemia & Lymphoma Society, said: "Managing an incurable blood cancer that progresses slowly can often feel indefinite and overwhelming. We welcome new treatment options that may ease the burden, restore a sense of control and offer renewed hope for those navigating life with chronic lymphocytic leukaemia."

Results from the AMPLIFY Phase III trial showed 77% of patients treated with *Calquence* plus venetoclax were progression free at three years, versus 67% of patients treated with standard-of-care chemotherapy (investigator's choice of fludarabine-cyclophosphamide-rituximab or bendamustine-rituximab).[2] Median progression-free survival (PFS) was not reached versus 47.6 months for chemoimmunotherapy.[2] Further, *Calquence* plus venetoclax reduced the risk of disease progression or death by 35% compared to chemoimmunotherapy (based on hazard ratio 0.65; 95% confidence interval 0.49-0.87; p=0.0038).[2]

Calquence plus venetoclax is approved in the European Union, Canada, UK and several other countries, and regulatory applications for the regimen based on the AMPLIFY results are currently under review in additional countries.

The safety and tolerability of *Calquence* was consistent with its known safety profile, and no new safety signals were identified.

Notes

Chronic lymphocytic leukaemia (CLL)

CLL is the most prevalent type of leukaemia in adults, with an estimated 40,000 people being treated for CLL in the first line in the US, UK, France, Germany, Spain, Italy, Japan and China in 2024.[4] Although some people with CLL may not experience any symptoms at diagnosis, others may experience symptoms, such as weakness, fatigue, weight loss, chills, fever, night sweats, swollen lymph nodes and abdominal pain.[5] In CLL, there is an accumulation of abnormal lymphocytes within the blood, bone marrow and lymph nodes. As the number of abnormal cells increases, there is less room within the marrow for the production of normal white blood cells, red blood cells and platelets.[3] This could result in infection, anaemia and bleeding. B-cell receptor signalling through BTK is one of the essential growth pathways for CLL.

AMPLIFY

AMPLIFY is a randomised, global, multi-centre, open-label Phase III trial evaluating the efficacy and safety of *Calquence* in combination with venetoclax, with or without obinutuzumab, compared to investigator's choice of chemoimmunotherapy (fludarabine-cyclophosphamide-rituximab or bendamustine-rituximab) in adult patients with previously untreated CLL without del(17p) or *TP53* mutation.[6] Patients were randomised 1:1:1 to receive either *Calquence* plus venetoclax, or *Calquence* plus venetoclax with obinutuzumab for a fixed duration, or standard-of-care chemoimmunotherapy.[6] Both the *Calquence* containing arms were administered for a fixed duration of 14 cycles (each 28 days), and the standard-of-care chemoimmunotherapy was administered for 6 cycles.[6]

The primary endpoint is PFS in the *Calquence* and venetoclax arm as assessed by an Independent Review Committee, and PFS is a key secondary endpoint in the *Calquence* plus venetoclax with obinutuzumab arm.[7] Other

key secondary endpoints include overall survival (OS) and undetectable measurable residual disease.[b] The trial includes 27 countries across North and South America, Europe, Asia and Oceania.[6]

The AMPLIFY trial enrolled patients from 2019 to 2021, continuing through the COVID-19 pandemic.[6]

Calquence
Calquence (acalabrutinib) is a second-generation, selective inhibitor of Bruton's tyrosine kinase (BTK). *Calquence* binds covalently to BTK, thereby inhibiting its activity.[7] In B-cells, BTK signalling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis and adhesion.

Calquence is approved for the treatment of chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL) in the US, Japan and China, and approved for CLL in Europe and many other countries. *Calquence* is also approved as a fixed-duration treatment for the treatment of adult patients with previously untreated CLL in combination with venetoclax in the US, and in combination with venetoclax, with or without obinutuzumab, in Europe, Canada, the U.K. and several other countries. *Calquence* is also approved for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) in the US, Europe, Japan and other countries. It is also approved for the treatment of adult patients with MCL who have received at least one prior therapy in China and several other countries.

As part of an extensive clinical development programme, *Calquence* is currently being evaluated as a single treatment and in combination with standard-of-care chemoimmunotherapy for patients with multiple B-cell blood cancers, including CLL, MCL and diffuse large B-cell lymphoma.

AstraZeneca in haematology
AstraZeneca is pushing the boundaries of science to redefine care in haematology. Our goal is to help transform the lives of patients living with malignant, rare and other related haematologic diseases through innovative medicines and approaches that are shaped by insights from patients, caregivers and physicians.

In addition to our marketed products, we are spearheading the development of novel therapies designed to target underlying drivers of disease across multiple scientific platforms. Our acquisitions of Alexion, with expertise in rare, non-malignant blood disorders, and Gracell Biotechnologies Inc., pioneers of autologous cell therapies, expand our haematology pipeline and enable us to reach more patients with high unmet needs through the end-to-end discovery, development and delivery of novel therapies.

AstraZeneca in oncology
AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

AstraZeneca
AstraZeneca (LSE/STO/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Social Media @AstraZeneca.

Contacts
For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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