Fixed-duration Calquence approved in EU for 1L CLL

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Fixed-duration *Calquence*-based regimens approved in EU for patients with chronic lymphocytic leukaemia in the 1st-line setting

AMPLIFY Phase III trial results demonstrated statistically significant and clinically meaningful improvement in progression-free survival for Calquence combinations

A fixed-duration regimen of AstraZeneca's *Calquence* (acalabrutinib) in combination with venetoclax, with or without obinutuzumab, has been approved in the European Union (EU) for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).

The approval by the European Commission follows the positive opinion of the Committee for Medicinal Products for Human Use and was based on positive results from the pivotal AMPLIFY Phase III trial, presented at the American Society of Hematology 2024 Annual Meeting and published in *The New England Journal of Medicine*.[1]

Results from the AMPLIFY trial showed 77% of patients treated with *Calquence* plus venetoclax and 83% of patients treated with *Calquence* plus venetoclax and obinutuzumab were progression free at three years, versus 67% of patients treated with standard-of-care chemoimmunotherapy (investigator's choice of fludarabine-cyclophosphamide-rituximab or bendamustine-rituximab).[1] Median progression-free survival (PFS) was not reached for either experimental arm versus 47.6 months for chemoimmunotherapy.[1] *Calquence* plus venetoclax reduced the risk of disease progression or death by 35% compared to chemoimmunotherapy (hazard ratio [HR] 0.65; 95% confidence interval [CI] 0.49-0.87; p=0.0038). *Calquence* plus venetoclax with obinutuzumab demonstrated a 58% reduction in the risk of disease progression or death compared to chemoimmunotherapy (HR 0.42; 95% CI 0.30-0.59; p<0.0001).[2]

CLL is the most common type of leukaemia in adults. An estimated 27,000 people were diagnosed with CLL in the UK, France, Germany, Spain and Italy in 2024.[3]

Barbara Eichhorst, MD, University Hospital Cologne, Cologne, Germany and investigator for the AMPLIFY trial, said: "For patients diagnosed with chronic lymphocytic leukaemia, this approval provides a new option in the first-line setting that may help to minimize long-term side effects and reduce drug resistance as they may occur with continuous treatment. A fixed-duration regimen is appealing to patients and helps with adherence during the treatment period."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "Today's approval brings a new fixed-duration treatment option to patients with previously untreated chronic lymphocytic leukaemia across Europe. *Calquence* plus venetoclax is the first and only all-oral combination treatment option with a second-generation BTK inhibitor approved in the EU and provides patients and their physicians more flexibility in managing this incurable blood cancer."

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

Regulatory applications for these regimens are currently under review in several countries based on the AMPLIFY results.

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.[3] 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.[4] 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.[5] 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 for 6 cycles.[6]

The primary endpoint is PFS in the *Calquence* and venetoclax arm as assessed by an Independent Review Committee, and PFS in the *Calquence* plus venetoclax with obinutuzumab arm is a key secondary endpoint.[6] Other key secondary endpoints include overall survival (OS) and undetectable measurable residual disease.[6] 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.[8] 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 the EU and many other countries. *Calquence* is also approved in combination with venetoclax, with or without obinutuzumab, as a fixed-duration treatment for CLL in the EU. *Calquence* is also approved for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) in the US, Europe 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. *Calquence* is not currently approved for the treatment of MCL in Japan.

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
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Contacts

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