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AstraZeneca PLC
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**Fixed-duration *Calquence*-based regimens recommended for approval in the EU by CHMP for 1st-line chronic lymphocytic leukaemia**

***Recommendation based on AMPLIFY Phase III trial which showed Calquence combinations demonstrated statistically significant and clinically meaningful improvement in progression-free survival vs. chemoimmunotherapy***

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

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on results from the AMPLIFY Phase III trial, which were presented at the American Society of Haematology (ASH) 2024 Annual Meeting and published in *The New England Journal of Medicine*.[1]

Results showed *Calquence* plus venetoclax reduced the risk of disease progression or death by 35% compared to standard-of-care chemoimmunotherapy (investigator's choice of fludarabine-cyclophosphamide-rituximab or bendamustine-rituximab; 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 standard-of-care chemoimmunotherapy (HR 0.42; 95% CI 0.30-0.59; p<0.0001).[2]

At three years, 77% of patients treated with *Calquence* plus venetoclax and 83% of patients treated with *Calquence* plus venetoclax and obinutuzumab were progression free, versus 67% of patients treated with chemoimmunotherapy.[1] Median progression-free survival (PFS) was not reached for either experimental arm versus 47.6 months for chemoimmunotherapy.[1]

Wojciech Jurczak, MD, Maria Sklodowska-Curie National Institute of Oncology, Kraków, Poland and investigator for the trial, said: "Chronic lymphocytic leukaemia is an incurable cancer which means patients live with the disease and stay on treatment for many years, which can have long-term effects. The fixed-duration *Calquence* regimens will allow patients to take breaks from their treatment, reducing the risk of long-term adverse events and drug resistance."

Susan Galbraith, Executive Vice President, Oncology Haematology R&D, AstraZeneca, said: "With this recommendation, *Calquence* plus venetoclax can potentially be the only all-oral second-generation BTK inhibitor option approved in Europe for patients with previously untreated chronic lymphocytic leukaemia. *Calquence* has demonstrated efficacy and safety in fixed-duration and treat-to-progression regimens providing patients and their doctors more treatment flexibility."

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

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

Regulatory applications for *Calquence* plus venetoclax, with or without obinutuzumab, in this setting 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 over 117,000 new cases globally in 2021.[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.[6] 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.[7] Patients were randomised 1:1:1 to receive either *Calquence* plus venetoclax, *Calquence* plus venetoclax with obinutuzumab for a fixed duration or standard-of-care chemoimmunotherapy.[7] 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.[7]

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 is a key secondary endpoint.[7] Other key secondary endpoints include OS and undetectable measurable residual disease.[7] The trial includes 27 countries across North and South America, Europe, Asia and Oceania.[7]

The AMPLIFY trial enrolled patients from 2019 to 2021, continuing through the COVID-19 pandemic.[7] Patients with blood cancer remain at a disproportionately high risk of severe outcomes from COVID-19, including hospitalisation

and death compared to the general population.[8]

***Calquence***
*Calquence* (acalabrutinib) is a second-generation, selective inhibitor of Bruton's tyrosine kinase (BTK). Calquence binds covalently to BTK, thereby inhibiting its activity.[9] 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, approved for CLL in the EU and many other countries worldwide. Calquence is also approved for the treatment of adult patients with previously untreated MCL in the US 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
For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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