Calquence recommended for EU approval in 1L MCL

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Calquence plus chemoimmunotherapy recommended for approval in the EU by CHMP as first and only BTK inhibitor for 1st-line mantle cell lymphoma

Recommendation based on ECHO Phase III trial results which demonstrated over 16 months of progression-free survival improvement vs. chemoimmunotherapy alone

AstraZeneca's *Calquence* (acalabrutinib) in combination with bendamustine and rituximab has been recommended for approval in the European Union (EU) for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are not eligible for autologous hematopoietic stem cell transplantation.

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on the results from the ECHO Phase III trial which were presented at the European Hematology Association 2024 Congress.

Results from the ECHO trial showed *Calquence* plus bendamustine and rituximab reduced the risk of disease progression or death by 27% compared to standard-of-care chemoimmunotherapy (hazard ratio [HR] 0.73; 95% confidence interval [CI] 0.57-0.94; p=0.016). Median progression-free survival (PFS) was 66.4 months for patients treated with the *Calquence* combination versus 49.6 with chemoimmunotherapy alone.

This recommendation for *Calquence* as a combination treatment in the 1st-line MCL setting follows the recent CHMP positive opinion for *Calquence* as a monotherapy for the treatment of adult patients with relapsed or refractory MCL.

Martin Dreyling, MD, Department of Medicine, University Hospital LMU Munich, and investigator in the trial, said: "Results from the pivotal ECHO trial demonstrated the significant benefits of the *Calquence* combination in managing this rare and aggressive cancer. Today's recommendation is an important advance within the mantle cell lymphoma first-line treatment landscape, especially for older patients who need a balance of efficacy and tolerability."

Susan Galbraith, Executive Vice President, Oncology Haematology R&D, AstraZeneca, said: "Today's positive recommendation from the CHMP further reinforces the potential of *Calquence* to advance first-line treatment options in mantle cell lymphoma, with the *Calquence* combination demonstrating an almost one and a half year improvement in progression-free survival in this setting. If approved, *Calquence* has the potential to transform the standard of care as the first BTK inhibitor approved for these patients in Europe."

MCL is a rare and typically aggressive form of non-Hodgkin lymphoma, often diagnosed at an advanced stage.[1,2] It is estimated that more than 6,000 patients were diagnosed with MCL 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.

Calquence plus bendamustine and rituximab is approved in the US and several other countries in this setting based on the ECHO results. Regulatory applications are currently under review in Japan and several other countries in this indication.

Notes

Mantle cell lymphoma (MCL)
While MCL patients initially respond to treatment, patients do tend to relapse.[4] MCL comprises about 3-6% of non-Hodgkin lymphomas, with an annual incidence of 0.5 per 100,000 population in Western countries; It is estimated that there are more than 21,000 patients diagnosed with MCL in the US, UK, France, Germany, Spain, Italy, Japan and China.[5]

ECHO
ECHO is a randomised, double-blind, placebo-controlled, multi-centre Phase III trial evaluating the efficacy and safety of *Calquence* plus bendamustine and rituximab compared to SoC chemoimmunotherapy (bendamustine and rituximab) in adult patients at or over 65 years of age (n=635) with previously untreated MCL.[6] Patients were randomised 1:1 to receive either *Calquence* or placebo administered orally twice per day, continuously, until disease progression or unacceptable toxicity. Additionally, all patients received six 28-day cycles of bendamustine on days 1 and 2 and rituximab on day 1 of each cycle, followed by rituximab maintenance for two years if patients achieved a response after induction therapy.[6]

The primary endpoint is PFS assessed by an Independent Review Committee; other efficacy endpoints include overall survival (OS), overall response rate (ORR), duration of response (DoR) and time to response (TTR).[6] The trial was conducted in 27 countries across North and South America, Europe, Asia and Oceania.[6]

The ECHO trial enrolled patients from May 2017 to March 2023, continuing through the COVID-19 pandemic. Prespecified PFS and OS analyses censoring for COVID-19 deaths were conducted to assess the impact of COVID-19 on the study outcome in alignment with the FDA. 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.[6,7,8]

Calquence
Calquence (acalabrutinib) is a second-generation, selective inhibitor of Bruton's tyrosine kinase (BTK). *Calquence* binds covalently to BTK, thereby inhibiting its activity.[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 and Japan, approved for CLL in the EU and many other countries worldwide and approved in China for relapsed or refractory CLL and SLL. *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 the US, 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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References

1. Lymphoma Research Foundation. Mantle Cell Lymphoma. Available at: http://lymphoma.org/aboutlymphoma/nhl/mcl/. Accessed March 2025.
2. National Organization for Rare Disorders. Mantle Cell Lymphoma. Available at: http://rarediseases.org/rare-diseases/mantle-cell-lymphoma/. Accessed March 2025.
3. AstraZeneca 2024. Q3 2024 Financial Results. Available at: http://www.astrazeneca.com/investor-relations.html. Accessed March 2025.
4. Cheah C, Seymour J, Wang ML. Mantle cell lymphoma. *J Clin Oncol*. 2016;34(11):1256-1269. doi: 10.1200/JCO.2015.63.5904.
5. Lynch DT, Koya S, Acharya U, et al. Mantle Cell Lymphoma. Available at: http://www.ncbi.nlm.nih.gov/books/NBK536985. Accessed March 2025.
6. ClinicalTrials.gov. A Study of BR Alone Versus in Combination With Acalabrutinib in Subjects With Previously Untreated MCL. Available at: http://clinicaltrials.gov/study/NCT02972840. Accessed March 2025.
7. Luque-Paz D, et al. B-cell malignancies and COVID-19: a narrative review. *Clin Microbiology and Infection*. 2023; 29(332-337).
8. Wu J, et al. Acalabrutinib (ACP-196): a selective second-generation BTK inhibitor. *J Hematol Oncol*. 2016;9(21).

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