AstraZeneca

Calquence approved in Japan for CLL

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Calquence approved in Japan for the treatment of relapsed or refractory chronic lymphocytic leukaemia

88% of patients on Calquence remained free of disease progression after 12 months vs. 68% for comparators

AstraZeneca's *Calquence* (acalabrutinib), a next-generation, selective Bruton's tyrosine kinase (BTK) inhibitor, has been approved in Japan for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) (including small lymphocytic lymphoma [SLL]).

The approval by the Japanese Ministry of Health, Labour and Welfare was based on positive results from the ASCEND Phase III trial and a Phase I trial in Japanese patients, showing *Calquence* monotherapy demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) versus a standard treatment of rituximab, a monoclonal antibody, combined with the physician's choice of idelalisib, a PI3-kinase inhibitor or bendamustine, a chemotherapy.

In the ASCEND trial, *Calquence* reduced the risk of disease progression or death by 69% (hazard ratio, 0.31; 95% confidence interval, 0.20-0.49, p<0.0001). These results were published in *Journal of Clinical Oncology* in 2020.[1]

CLL is the most common type of adult leukaemia across the globe but is considered a rare disease in Japan and East Asia, representing between 1% and 2% of patients diagnosed with leukaemia.[2-4]

Dai Maruyama, MD, PhD, Director, Department of Hematology and Oncology, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan said: "Today's news marks great progress for patients with chronic lymphocytic leukaemia in Japan. As the ASCEND trial showed, *Calquence* provides a significant improvement in progression-free survival compared with current standard therapies. Treatment with a safe and tolerable regimen remains paramount for these patients who often require ongoing therapy for many years."

Dave Fredrickson, Executive Vice President, Oncology Business Unit, said: "Chronic lymphocytic leukaemia is less prevalent in Japan than other regions, yet patients remain in need of innovative treatment options. This approval of *Calquence* offers patients in Japan a new, chemo-free, tolerable treatment option with uncompromised efficacy and the potential to positively impact quality of life."

In the ASCEND Phase III trial, an estimated 88% of patients with relapsed or refractory CLL treated with *Calquence* remained alive and free from disease progression after 12 months compared with 68% of patients on rituximab combined with idelalisib or bendamustine. After a median follow up of 16.1 months, median PFS was not reached with *Calquence* monotherapy versus 16.5 months in the control arm.[1]

The safety and tolerability of *Calquence* were consistent with its established profile.[1] Final results of the ASCEND Phase III trial were presented at the 2020 American Society of Clinical Oncology and 2020 European Hematology Association virtual meetings and demonstrated the long-term (median 22-month follow-up) efficacy and tolerability of *Calquence* in CLL.[5,6]

Calquence is approved for the treatment of CLL and SLL in the US and is approved for the treatment of CLL in the EU and in several other countries worldwide in the 1st-line and relapsed or refractory settings. *Calquence* is also approved in the US and several other countries for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. *Calquence* is not currently approved for the treatment of MCL in Japan or the EU.

As part of a broad development programme, *Calquence* is being assessed in more than 20 AstraZeneca-sponsored clinical trials for the treatment of patients with B-cell malignancies including CLL, MCL, diffuse large B-cell lymphoma, Waldenström's macroglobulinaemia, follicular lymphoma, and other haematologic malignancies.

A Japanese Phase I/II trial based on the ELEVATE TN Phase III trial is currently underway for the treatment of 1st-line CLL.

CLL

CLL is the most common type of leukaemia in adults, with an estimated 114,000 new cases globally in 2017, and the number of people living with CLL is expected to grow with improved treatment as patients live longer with the disease.[7-10] In CLL, too many blood stem cells in the bone marrow become abnormal lymphocytes and these abnormal cells have difficulty fighting infections. As the number of abnormal cells grows there is less room for healthy white blood cells, red blood cells, and platelets. This could result in anaemia, infection, and bleeding.[7] B-cell receptor signalling through BTK is one of the essential growth pathways for CLL.

ASCEND

ASCEND (ACE-CL-309) was a global, randomised, multicentre, open-label Phase III trial evaluating the efficacy of *Calquence* in patients with relapsed or refractory CLL. In the trial, 310 patients were randomised (1:1) into two arms. Patients in the first arm received *Calquence* monotherapy (100mg twice daily until disease progression or unacceptable toxicity). Patients in the second arm received physician's choice of either rituximab, a CD20 monoclonal antibody, in combination with idelalisib, a PI3-kinase inhibitor, or rituximab in combination with bendamustine, a chemotherapy.[1]

The primary endpoint was PFS assessed by an Independent Review Committee (IRC), and key secondary endpoints included investigator-assessed PFS, IRC- and investigator-assessed overall response rate and duration of response, as well as overall survival, patient-reported outcomes and time to next treatment.[1] ASCEND is the first randomised Phase III trial to directly compare a BTK inhibitor as monotherapy to these combinations in relapsed or refractory CLL.

AstraZeneca in haematology

Leveraging its strength in oncology, AstraZeneca has established haematology as one of four key oncology disease areas of focus. The Company's haematology franchise includes two medicines approved in the US and a robust global development programme for a broad portfolio of potential blood cancer treatments. Acerta Pharma serves as AstraZeneca's haematology research and development arm. AstraZeneca partners with like-minded science-led companies to advance the discovery and development of therapies to address unmet need.

AstraZeneca in oncology

AstraZeneca has a deep-rooted heritage in oncology and offers a quickly growing portfolio ofnew medicines that has the potential to transform patients' lives and the Company's future. With seven new medicines launched between 2014 and 2020, and a broad pipelineof small molecules and biologics in development, the Company is committed to advance oncology as a key growth driver for AstraZeneca focused on lung, ovarian, breast and blood cancers.

By harnessing the power of six scientific platforms - Immuno-Oncology, Tumour Drivers and Resistance, DNA Damage Response, Antibody Drug Conjugates, Epigenetics, and Cell Therapies - and by championing the development of personalised combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

AstraZeneca

AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

Contacts

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

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