AstraZeneca

Calquence met primary endpoint against ibrutinib

25 January 2021 07:00 GMT

Calquence met primary efficacy endpoint in head-to-head trial against ibrutinib in chronic lymphocytic leukaemia

Superior safety on key secondary endpoint of atrial fibrillation

Positive high-level results from the ELEVATE-RR Phase III trial showed AstraZeneca's *Calquence* (acalabrutinib) met the primary endpoint demonstrating non-inferior progression-free survival (PFS) for adults with previously treated, high-risk chronic lymphocytic leukaemia (CLL) compared to ibrutinib.

The trial also met a key secondary endpoint for safety, showing patients treated with *Calquence* had statistically significantly lower incidence of atrial fibrillation compared to patients treated with ibrutinib. Atrial fibrillation is an irregular heart rate that can increase the risk of stroke, heart failure and other heart-related complications.[1] Further hierarchical testing revealed no difference for Grade 3 or higher infections or Richter's transformation. There was a descriptive trend for numerically favourable overall survival. Overall, the safety and tolerability of *Calquence* were consistent with the profile seen in the broader *Calquence* clinical development programme.

ELEVATE-RR is the first Phase III trial to compare two Bruton's tyrosine kinase (BTK) inhibitors in patients with CLL, the most common type of leukaemia in adults.[2] Patients diagnosed with high-risk CLL may experience rapid worsening of their disease, requiring treatment.[3]

José Baselga, Executive Vice President, Oncology R&D, said: "With over forty months of follow-up, today's results confirm that *Calquence*, a selective BTK inhibitor, displays superior safety in atrial fibrillation without compromising efficacy. The totality of the data confirm our confidence in the favourable benefit-risk profile of *Calquence.*"

The data will be presented at a forthcoming medical meeting and shared with health authorities.

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.[2,4-6] 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.[4] B-cell receptor signalling through BTK is one of the essential growth pathways for CLL.

ELEVATE-RR

ELEVATE-RR (ACE-CL-006) is a randomised, multicentre, open-label Phase III non-inferiority trial of *Calquence* versus ibrutinib in patients with previously treated CLL with high-risk features (presence of 17p deletion and/or 11q deletion). In the trial, 533 patients were randomised (1:1) into two arms. Patients in the first arm received *Calquence* (100mg orally twice daily) until disease progression or unacceptable toxicity. Patients in the second arm received ibrutinib (420mg orally once daily) until disease progression or unacceptable toxicity.[7]

The primary endpoint for the trial was PFS assessed by an independent review committee (non-inferiority; tested after 250 events). Secondary endpoints included incidence of atrial fibrillation, incidence of treatment-emergent Grade 3 or higher infections, incidence of Richter's transformation (a condition in which CLL changes into an aggressive form of lymphoma) and overall survival.[7]

Calquence

Calquence (acalabrutinib) is a next-generation, selective inhibitor of BTK. *Calquence* binds covalently to BTK, thereby inhibiting its activity.[8,9] In B-cells, BTK signalling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion.[8]

Calquence is approved for the treatment of CLL and small lymphocytic lymphoma in the US and approved for CLL in the EU and several other countries worldwide. *Calquence* is under regulatory review in Japan for relapsed or refractory CLL. A Phase I trial is currently underway in Japan for the treatment of 1st-line CLL.

In the US and several other countries, *Calquence* is also approved for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. The US MCL indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. *Calquence* is not currently approved for the treatment of MCL in Europe or Japan.

As part of an extensive clinical development programme, AstraZeneca and Acerta Pharma are currently evaluating *Calquence* in more than 20 company-sponsored clinical trials. *Calquence* is being developed for the treatment of multiple B-cell blood cancers including CLL, MCL, diffuse large B-cell lymphoma, Waldenström's macroglobulinaemia, follicular lymphoma, and other haematologic malignancies.

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 of new 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 pipeline of 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.

References

1. Mayo Clinic. Patient Care & Health Information, Diseases & Conditions - Atrial Fibrillation.

Available at: https://www.mayoclinic.org/diseases-conditions/atrial-fibrillation/symptoms-causes/. Accessed January 2021.

2. American Cancer Society. What is Chronic Lymphocytic Leukemia. Available at: https://www.cancer.org/cancer/chronic-lymphocytic-leukemia/about/what-is-cll.html. Accessed January 2021.

3. Cancer.net. Leukemia-Chronic Lymphocytic - CLL: Stages. Available at: https://www.cancer.net/cancer-types/leukemia-chronic-lymphocytic-cll/stages. Accessed January 2021.

4. National Cancer Institute. Chronic Lymphocytic Leukemia Treatment (PDQ®)-Patient Version. Available at: https://www.cancer.gov/types/leukemia/patient/cll-treatment-pdq. Accessed January 2021.

5. Global Burden of Disease Cancer Collaboration. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017. *JAMA Oncol*. 2019;5(12):1749-1768.

6. Jain N, *et al*. Prevalence and Economic Burden of Chronic Lymphocytic Leukemia (CLL) in the Era of Oral Targeted Therapies. *Blood*. 2015;126:871.5.

7. Clinicaltrials.gov. NCT02477696. Accessed September 18, 2020. Study started in October 2015.

8. CALQUENCE (acalabrutinib) [U.S. prescribing information]. Wilmington, DE; AstraZeneca Pharmaceuticals LP; 2019.

9. Wu J, Zhang M & Liu D. Acalabrutinib (ACP-196): a selective second-generation BTK inhibitor. *J Hematol Oncol*. 2016;9(21).

Adrian Kemp

Company Secretary

AstraZeneca PLC