AstraZeneca

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Calquence data across four trials reinforces cardiovascular safety profile in patients with chronic lymphocytic leukaemia

Less than 1% of patients treated with Calquence discontinued treatment due to cardiac adverse events in pooled analysis

A pooled analysis of cardiovascular (CV) safety data from 762 patients treated with *Calquence* (acalabrutinib) monotherapy for chronic lymphocytic leukaemia (CLL), the most common type of adult leukaemia, across four clinical trials showed a low incidence of cardiac adverse events (AEs) leading

to discontinuation.[1,2] These results were presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition on 7 December 2020.

The analysis included patients with previously untreated and relapsed or refractory CLL treated with *Calquence* alone from the ELEVATE TN and ASCEND Phase III trials, as well as the 15-H-0016 Phase II trial and ACE-CL-001 Phase I/II trial. In the analysis, 129 patients (17%) reported a cardiac AE of any grade at a median follow up of 25.9 months, and seven patients (0.9%) discontinued treatment due to cardiac AEs.[1]

Jennifer Brown, MD, PhD, Director of the CLL Center of the Division of Hematologic Malignancies, Dana-Farber Cancer Institute, and principal investigator, said: "Cardiac adverse events have emerged as an important consideration for treating chronic lymphocytic leukaemia patients with Bruton's tyrosine kinase inhibitors, as cardiovascular complications have become a frequent reason for discontinuation. The data presented in this study suggests a low risk of cardiac adverse events with acalabrutinib that is similar to those in a general population of untreated patients with chronic lymphocytic leukaemia, giving clinicians further reassurance when prescribing this therapy."

José Baselga, Executive Vice President, Oncology R&D, said: "These combined results across four of our clinical trials reinforce the cardiovascular safety profile of *Calquence* for the treatment of chronic lymphocytic leukaemia. With *Calquence*, we aim to selectively target Bruton's tyrosine kinase to help improve safety and long-term adherence while maintaining outstanding efficacy."

Median exposure to *Calquence* was 24.9 months. Cardiac events that occurred in 2% or more of patients included atrial fibrillation (4%), atrial fibrillation/flutter (5%), palpitations (3%) and tachycardia (2%). The incidence of atrial fibrillation was similar to that in a general, previously untreated CLL patient population (6%).[1,3]

Grade 3 or higher cardiac AEs occurred in 37 patients (4%) treated with *Calquence* monotherapy, of which 25% were reported during the first six months of treatment. Grade 3 or higher cardiac AEs of interest included atrial fibrillation (1.3%), complete atrioventricular (AV) block (0.3%), acute coronary syndrome (0.1%), atrial flutter (0.1%), second degree AV block (0.1%) and

ventricular fibrillation (0.1%). Two patients experienced Grade 5 AEs (one with congestive heart failure and one with heart attack).[1]

Overall, 91% of patients with cardiac AEs versus 79% patients without cardiac AEs had one or more CV risk factors before receiving *Calquence*. The most prevalent CV risk factors (greater than or equal to 20% of patients) among those who experienced cardiac AEs were hypertension (67%), hyperlipidemia (29%) and arrhythmias (22%).[1]

AstraZeneca is exploring additional trials in CLL, including the ELEVATE-RR Phase III trial (ACE-CL-006) evaluating *Calquence* versus ibrutinib in patients with previously treated high-risk CLL. Data is anticipated in 2021.

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in adults, with an estimated 105,000 new cases globally in 2016, and the number of people living with CLL is expected to grow with improved treatment as patients live longer with the disease.[2,4,5,6] 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 Bruton's tyrosine kinase (BTK) is one of the essential growth pathways for CLL.

Calquence

Calquence (acalabrutinib) is a next-generation, selective inhibitor of BTK. *Calquence* binds covalently to BTK, thereby inhibiting its activity.[7,8] In B-cells, BTK signalling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion.[7]

Calquence is approvedfor the treatment of CLL and small lymphocytic lymphoma in the US and is approved for CLL in the EU and several other countries worldwide. *Calquence* is also approved for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy in the US and several other countries.

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 by the US Food and Drug Administration 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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Om AstraZeneca

AstraZeneca är ett globalt, innovationsdrivet bioläkemedelsföretag med fokus på forskning, utveckling och marknadsföring av receptbelagda läkemedel, primärt för behandling av sjukdomar inom tre huvudsakliga terapiområden: cancer, kardiovaskulära sjukdomar, njursjukdomar och metabola sjukdomar och sjukdomar i andningsvägarna. AstraZeneca bedriver verksamhet i över 100 länder och dess innovativa läkemedel används av miljontals patienter över hela världen.

Mer information finns på: www.astrazeneca.com och www.astrazeneca.se. Du kan även följa oss på twitter https://twitter.com/AstraZenecaSE

Kontaktpersoner

Christina Malmberg Hägerstrand
Presskontakt
Presschef, AstraZeneca AB och Norden-Baltikum
christina.malmberghagerstrand@astrazeneca.com
+46 8 552 531 06
+46 72 855 93 29

Jacob Lund
Presskontakt
Kommunikationsdirektör AstraZeneca Norden, Baltikum och ordförande Leif Johanssons kontor
jacob.lund@astrazeneca.com
08 553 260 20 Mobil: 072 560 21 57