News Release

Regulatory News Service

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Calquence significantly prolonged the time patients lived without disease progression in relapsed or refractory chronic lymphocytic leukaemia

An encouraging 88% of patients on Calquence remained free of disease progression after 12 months, vs. 68% of patients on rituximab combined with idelalisib or bendamustine

AstraZeneca today announced detailed results from the interim analysis of the Phase III ASCEND trial at the European Hematology Association (EHA) Annual Congress in Amsterdam, showing *Calquence* (acalabrutinib) significantly prolonged the time patients live without disease progression in relapsed or refractory chronic lymphocytic leukaemia (CLL).

The ASCEND trial compared *Calquence* with the physician's choice of rituximab combined with idelalisib (IdR) or bendamustine (BR) in patients with relapsed or refractory CLL.

At a median follow-up of 16.1 months, results from the trial showed a statistically-significant and clinically-meaningful improvement in progression-free survival (PFS) for patients treated with *Calquence* vs. IdR or BR, reducing the risk of disease progression or death by 69% (HR, 0.31; 95% CI, 0.20-0.49, p<0.0001). The median time without disease progression for patients treated with *Calquence* has not yet been reached vs. 16.5 months in the control arm. At 12 months, 88% of patients on *Calquence* showed no disease progression compared to 68% for the control arm. The safety and tolerability of *Calquence* was consistent with its established profile.

José Baselga, Executive Vice President, Oncology R&D said: "These data add to the growing body of evidence to support the profile of *Calquence* as a selective BTK inhibitor that offers a chemotherapy-free treatment option with a favourable safety profile in chronic lymphocytic leukaemia, a life-threatening disease. These data, along with our recent positive results from the Phase III ELEVATE-TN trial in previously-untreated chronic lymphocytic leukaemia, will serve as the foundation for regulatory submissions later this year."

Paolo Ghia, MD, Professor, Medical Oncology, Università Vita-Salute San Raffaele in Milan, and investigator of the ASCEND trial, said: "This is the first randomised trial to directly compare a BTK inhibitor as monotherapy with standard chemoimmunotherapy or idelalisib and rituximab combinations. With a significant improvement in progression-free survival and a favourable safety profile, acalabrutinib may become an important choice for the treatment of patients with relapsed or refractory chronic lymphocytic leukaemia."

Kaplan-Meier plot for PFS as assessed by an independent review committee in the intent-to-treat population[1]

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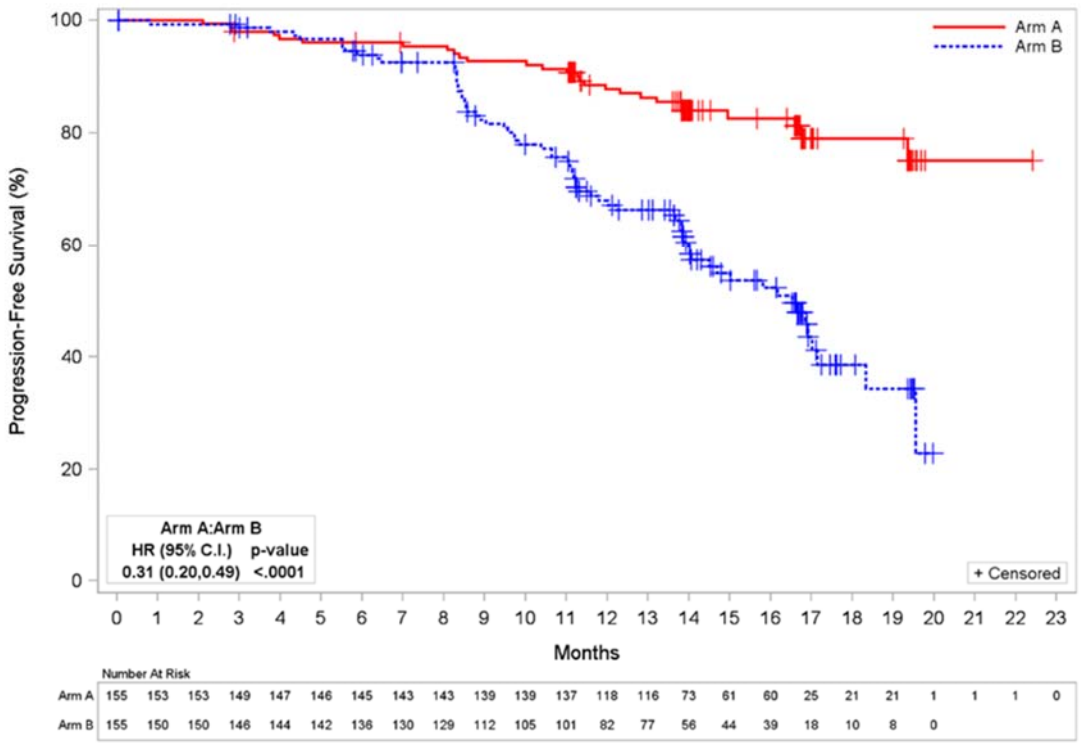

Calquence (arm A) vs IdR or BR (arm B)

Safety overview

Most common (≥15%) AEs, n (%)	***Calquence* (n=154)**		**IdR (n=118)**		**BR (n=35)**	
	Any	Grade ≥3	Any	Grade ≥3	Any	Grade ≥3
Headache	34 (22%)	1 (1%)	7 (6%)	0	0	0
Neutropenia	30 (19%)	24 (16%)	53 (45%)	47 (40%)	12 (34%)	11 (31%)
Diarrhoea	28 (18%)	2 (1%)	55 (47%)	28 (24%)	5 (14%)	0
Anaemia	23 (15%)	18 (12%)	11 (9%)	8 (7%)	4 (11%)	3 (9%)
Cough	23 (15%)	0	18 (15%)	1 (1%)	2 (6%)	0
Pyrexia	19 (12%)	1 (1%)	21 (18%)	8 (7%)	6 (17%)	1 (3%)
Fatigue	15 (10%)	2 (1%)	10 (8%)	0	8 (23%)	1(3%)
Nausea	11 (7%)	0	15 (13%)	1 (1%)	7 (20%)	0
IRR	0	0	9 (8%)	2 (2%)	8 (23%)	1 (3%)
Events of clinical interest for *Calquence*						
Atrial fibrillation	8 (5%)	2 (1%)	4 (3%)	1 (1%)	1 (3%)	1 (3%)
Bleeding	40 (26%)	3 (2%)	9 (8%)	3 (3%)	2 (6%)	1(3%)
Hypertension	5 (3%)	3 (2%)	5 (4%)	1 (1%)	0	0
SPM* excluding NMSC**	10 (6%)	5 (3%)	3 (3%)	0	1 (3%)	1 (3%)

*Secondary primary malignancy **Non-melanoma skin cancer.

AstraZeneca recently announced that the Phase III ELEVATE-TN trial met its primary endpoint at interim analysis in patients with previously-untreated CLL and that full results will be reported at a forthcoming medical meeting. *Calquence* is currently approved for the treatment

of adults with relapsed or refractory mantle cell lymphoma (MCL) in the US, Brazil, the United Arab Emirates, and Qatar and is being developed for the treatment of CLL and other blood cancers.

About ASCEND
ASCEND (ACE-CL-309) is a global, randomised, multicentre, open-label Phase III trial evaluating the efficacy of *Calquence* in previously-treated patients with CLL.[2] 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). Patients in the second arm received physician's choice of either rituximab in combination with idelalisib or rituximab in combination with bendamustine.[1,2]

The primary endpoint is PFS assessed by an independent review committee (IRC), and key secondary endpoints include physician-assessed PFS, IRC- and physician-assessed overall response rate (ORR) and duration of response (DoR), as well as overall survival (OS), patient reported outcomes (PROs) and time to next treatment (TTNT).[1,2]

About *Calquence*
Calquence (acalabrutinib) was granted accelerated approval by the US Food and Drug Administration (FDA) in October 2017 for the treatment of adult patients with MCL who have received at least one prior therapy. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Calquence is an inhibitor of Bruton tyrosine kinase (BTK). *Calquence* binds covalently to BTK, thereby inhibiting its activity.[3] In B-cells, BTK signalling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion.

As part of an extensive clinical development programme, AstraZeneca and Acerta Pharma are currently evaluating *Calquence* in 26 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, Waldenstrom macroglobulinaemia, follicular lymphoma, and multiple myeloma and other haematologic malignancies. Beyond the positive Phase III trials ASCEND and ELEVATE-TN, other Phase III trials in CLL are ongoing, including ELEVATE-RR (ACE-CL-006) evaluating acalabrutinib vs. ibrutinib in patients with previously-treated high-risk CLL, and ACE-CL-311 evaluating acalabrutinib in combination with venetoclax and with/without obinutuzumab in patients with previously-untreated CLL without 17p deletion or TP53 mutation.

About chronic lymphocytic leukaemia
Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in adults, with an estimated 191,000 new cases globally and 20,720 new cases in the US annually, and prevalence that is expected to grow with improved treatment.[4-7] In CLL, too many blood stem cells in the bone marrow become abnormal lymphocytes and these abnormal cells have difficulty fighting infections.[4] As the number of abnormal cells grows there is less room for healthy white blood cells, red blood cells and platelets.[4] This could result in anaemia, infection and bleeding.[4] B-cell receptor signalling through BTK is one of the essential growth pathways for CLL.

About 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 US FDA-approved medicines 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.

In October 2018, AstraZeneca and Innate Pharma announced a global strategic collaboration that included Innate Pharma licensing the US commercial rights of *Lumoxiti* (moxetumomab pasudotox-tdfk), and with support from AstraZeneca, will continue EU development and commercialisation, pending regulatory submission and approval.

About 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 at least six new medicines to be launched between 2014 and 2020, and a broad pipeline of small molecules and biologics in development, we are committed to advance oncology as a key growth driver for AstraZeneca focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy as illustrated by our investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms – Immuno-Oncology, Tumour Drivers and Resistance, DNA Damage Response and Antibody Drug Conjugates – 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.

About AstraZeneca
AstraZeneca 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. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca.com and follow us on Twitter @AstraZeneca.

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