News Release

AstraZeneca

EARLY DATA DEMONSTRATE CLINICAL ACTIVITY OF ACALABRUTINIB IN DIFFICULT-TO-TREAT CHRONIC LYMPHOCYTIC LEUKAEMIA

Phase I/II trial findings add to growing body of data on acalabrutinib clinical profile

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AstraZeneca and its haematology Centre of Excellence, Acerta Pharma, today announced preliminary results from the Phase I/II ACE-CL-001 clinical trial of acalabrutinib in subsets of patients with two difficult-to-treat forms of chronic lymphocytic leukaemia (CLL), the most common type of leukaemia in adults.[1] The trial includes data from individuals with intolerance to ibrutinib and those with Richter transformation, when CLL transforms into a more aggressive lymphoma.[2] Findings were shared with the medical community during two oral presentations at the 58th American Society of Hematology (ASH) Annual Meeting in San Diego, USA.

Acerta Pharma Chief Executive Officer, Flavia Borellini, PhD, said: "The data at ASH further validate previous clinical trial findings and continue to demonstrate the potential of acalabrutinib in the treatment of B-cell malignancies."

Investigator Jennifer R. Brown, MD, PhD and Director, Chronic Lymphocytic Leukemia Center, Dana-Farber Cancer Institute, said: "The acalabrutinib data in patients in difficult-to-manage settings support the continued exploration of acalabrutinib's potential for the treatment of CLL."

Acalabrutinib is an investigational, highly selective, potent Bruton tyrosine kinase (BTK) inhibitor shown to minimise off-target activity in pre-clinical studies.[3,4,5] The Phase I/II findings presented at ASH are part of an extensive and ongoing clinical development programme for acalabrutinib in B-cell cancers including CLL, mantle cell lymphoma (MCL), Waldenström macroglobulinemia, follicular lymphoma and diffuse large B-cell lymphoma.

Results for acalabrutinib in patients intolerant to ibrutinib

The ibrutinib-intolerant cohort included 33 patients with relapsed or refractory CLL intolerant to ibrutinib. In a population with difficult-to-treat disease and limited treatment options, a 79% overall response rate was achieved with acalabrutinib.[6] The median progression free survival has not yet been reached, with 81% of responding patients achieving a duration of response ≥12 months on acalabrutinib treatment,[6] which may allow for continuation of BTK inhibitor therapy.

In this cohort of patients, the most common adverse events included diarrhoea (52% overall; 0% ≥ Grade 3), headache (39% overall; 0% ≥ Grade 3), cough (24% overall; 0% ≥ Grade 3), increased weight (24% overall; 0% ≥ Grade 3) and nausea (21% overall; 0% ≥ Grade 3).[6] Serious adverse events occurred in 33% of patients.[6] Thirty six percent of patients had a recurrence of an adverse event they had experienced during previous treatment with ibrutinib, most of which were of decreased or the same severity.[6] No patients discontinued acalabrutinib due to a recurrent adverse event.[6]

Results for acalabrutinib in patients with aggressive transformation of CLL
A separate presentation showed preliminary data on the clinical activity of acalabrutinib monotherapy in a cohort of 29 patients with Richter transformation or other transformations—aggressive B-cell malignancies associated with an aggressive clinical course and poor prognosis.[7] Of the 21 Richter transformation patients evaluable for efficacy measures, the overall response rate was 38% and the median progression-free survival was 2.1 months (95% CI, 1.8 to 3.7).[7] The median duration of response on acalabrutinib treatment was 5.2 months (range 0.3 – 6.5+).[7]

In this cohort of patients, the most common adverse events were headache (41% overall; 0% ≥ Grade 3), diarrhoea (35% overall; 0% ≥ Grade 3), anaemia (31% overall; 14% ≥ Grade 3), fatigue (24% overall; 7% ≥ Grade 3), arthralgia (joint pain) (17% overall; 3% ≥ Grade 3) and back pain (17% overall; 10% ≥ Grade 3).[7] Serious adverse events occurred in 55% of patients. No patients discontinued acalabrutinib treatment due to adverse events.[7]

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NOTES TO EDITORS

About chronic lymphocytic leukaemia and Richter transformation
Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in adults and accounts for approximately one in four cases of leukaemia.[1,8] The average age at the time of diagnosis is approximately 71 years of age.[8] In CLL, too many blood stem cells in the bone marrow become abnormal lymphocytes and these abnormal cells have difficulty fighting infections.[9] As the number of abnormal cells grows there is less room for healthy white blood cells, red blood cells and platelets.[6] This could result in anaemia, infection and uncontrolled bleeding.[9] Approximately 2% to 10% of CLL patients develop Richter transformation, where CLL transforms into an aggressive lymphoma, most often diffuse large B-cell lymphoma.[10] Prognosis for patients with Richter transformation is poor, with median overall survival of approximately eight months.[11] B-cell receptor signalling through Bruton tyrosine kinase (BTK) is one of the essential growth pathways for CLL.

About acalabrutinib
Acalabrutinib (ACP-196) is an investigational, highly selective, potent Bruton tyrosine kinase (BTK) inhibitor, shown to minimise off-target activity in pre-clinical studies.[3,4,5] Studies of acalabrutinib have demonstrated clinical activity in monotherapy with an expected tolerability profile in people with previously untreated or relapsed or refractory CLL, including those with del17p.[4,12] Acalabrutinib is in ongoing clinical development for the treatment of a range of B-cell cancers including CLL, MCL, Waldenström macroglobulinemia, follicular lymphoma and diffuse large B-cell lymphoma, with both monotherapy and combination therapy strategies. The acalabrutinib development programme also includes monotherapy and combination studies in solid tumours. In total, more than 20 acalabrutinib clinical trials with more than 2,000 patients are underway.

About AstraZeneca and Acerta Pharma
Acerta Pharma, a member of the AstraZeneca Group, is a leader in the field of covalent binding technology and is applying this technology to create novel selective therapies intended for the treatment of cancer and autoimmune diseases. The company has operations in Oss, the Netherlands and multiple US sites. The US headquarters is in Redwood City, CA. For more information, please visit www.acerta-pharma.com.

AstraZeneca acquired a majority stake interest in Acerta Pharma and its cornerstone asset, acalabrutinib, in February 2016. Acerta Pharma serves as AstraZeneca's haematology Centre of Excellence.

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 New Oncology as one of AstraZeneca's six Growth Platforms 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, the genetic drivers of cancer 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 main therapy areas - Oncology, Cardiovascular & Metabolic Diseases and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. 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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