RNS Number : 1999R
AstraZeneca PLC
16 July 2025

16 July 2025

Update on CARES Phase III clinical programme of anselamimab in light chain amyloidosis

Results did not achieve statistical significance for the primary endpoint in overall patient population

Anselamimab showed highly clinically meaningful improvement vs. placebo in survival and cardiovascular hospitalisation in prespecified patient subgroup

High-level results from the Cardiac Amyloid Reaching for Extended Survival (CARES) Phase III clinical programme showed that anselamimab, a light chain depleter antibody, did not achieve statistical significance for the primary endpoint compared to placebo in patients with Mayo stages IIIa and IIIb light chain (AL) amyloidosis. The primary endpoint was defined as a hierarchical combination of time to all-cause mortality (ACM) and frequency of cardiovascular hospitalisations (CVH). All patients in the clinical programme received background standard of care for plasma cell dyscrasia.

Anselamimab showed highly clinically meaningful improvement in time to ACM and frequency of CVH in a prespecified subgroup of patients, compared to placebo.

AL amyloidosis is a rare, systemic and progressive disorder caused by defective plasma cells in the bone marrow. In AL amyloidosis, abnormal light chain proteins produced by these plasma cells misfold, aggregate and form amyloid fibrils that deposit in tissues and organs. Left untreated, the accumulation of these toxic amyloid deposits, particularly in the heart and kidneys, can cause progressive organ damage and dysfunction and may lead to premature death, most commonly due to cardiac failure.[1-3]

Ashutosh Wechalekar, MBBS, MD, FRCP, FRCPath, DM, Consultant Haematologist at University College London Hospitals NHS Foundation Trust (UCLH), Professor of Medicine and Haematology at University College London (UCL) and lead principal investigator of the programme, said: "While the study did not meet the primary endpoint in the overall patient population, results from a pre-defined subgroup suggest that anselamimab, by targeting and clearing amyloid deposits, may address a leading cause of organ damage and functional impairment in these patients. The potential to extend survival and reduce cardiovascular hospitalisations would represent a practice-changing advancement for this patient group."

Marc Dunoyer, Chief Executive Officer, Alexion, AstraZeneca Rare Disease, said: "Alexion is pioneering a novel mechanism of action to address organ damage from existing amyloid deposits in patients with AL amyloidosis, a devastating disease often diagnosed in advanced stages with poor prognosis. Anselamimab is the first and only investigational fibril depleter to show clinical benefit in AL amyloidosis, and these results underscore its potential to address a critical treatment gap in a prespecified subgroup of patients."

Anselamimab was well tolerated, with the majority of events balanced between the anselamimab treatment arm and the placebo arm.

Evaluation of full results is ongoing to further characterise the efficacy and safety of anselamimab. Alexion plans to share these data with global health authorities and present them at a forthcoming medical meeting.

Notes

Light Chain amyloidosis
Light chain (AL) amyloidosis is a systemic and progressive type of amyloidosis where immunoglobulin light chain proteins are produced abnormally by defective plasma cells in the bone marrow. These abnormal proteins misfold, aggregate and form amyloid fibrils that deposit and accumulate in tissues or organs, particularly in the heart and kidneys. The deposition can cause progressive damage and may lead to premature death, most commonly due to cardiac failure.[1,2]

In the early stages of the disease, people with AL amyloidosis may experience a range of vague signs and symptoms that mimic other diseases, which can often delay the diagnosis. Worldwide, there are an estimated 74,000 patients living with AL amyloidosis.[4,5]

CARES Phase III Clinical Programme
The Cardiac Amyloid Reaching for Extended Survival (CARES) clinical programme consists of two parallel global, Phase III, randomised, double-blind, placebo-controlled, multicentre trials evaluating the efficacy and safety of anselamimab plus standard of care (SoC) in patients with stage IIIa and stage IIIb light chain (AL) amyloidosis, respectively.[6,7]

The primary endpoint is a hierarchical combination of time to all-cause mortality and frequency of cardiovascular hospitalisations in the overall patient population across both trials.

The CARES clinical programme is the largest prospective investigation in cardiac AL amyloidosis to date with a total of 406 patients enrolled from 19 countries globally, including 281 patients with stage IIIa and 125 patients with stage IIIb disease per European modification of the Mayo 2004 staging system.[6,7]

In CARES, newly diagnosed patients planning first-line plasma cell dyscrasia (PCD) treatment with cyclophosphamide, bortezomib and dexamethasone were randomised 2:1 to receive either anselamimab or placebo once weekly for the first four weeks and then every two weeks until study completion. Daratumumab was permitted but not required as part of the PCD regimen, and approximately 80% of patients in CARES received daratumumab as part of their treatment.

Following the primary evaluation treatment period, which concluded 18 months after the last patient was randomised

Following the primary evaluation treatment period, which concluded 18 months after the last patient was randomised, all patients had the option to participate in an open-label extension period receiving anselamimab plus SoC for up to 24 months.[6,7]

Anselamimab
Anselamimab is an investigational, potentially first-in-class anti-fibril monoclonal antibody designed to improve organ function by reducing or eliminating amyloid deposits in the tissues and organs of patients living with AL amyloidosis. By binding with specificity to targets within amino acids on misfolded amyloid fibrils, anselamimab promotes destruction and clearance of amyloid deposits, while sparing native free light chains from destruction. Anselamimab has been granted Fast Track Designation by the US Food and Drug Administration (FDA) and received Orphan Drug Designation from the US FDA, European Commission and the Ministry of Health, Labour and Welfare of Japan for the treatment of AL amyloidosis.

Alexion
Alexion, AstraZeneca Rare Disease, is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and delivery of life-changing medicines. A pioneering leader in rare disease for more than three decades, Alexion was the first to translate the complex biology of the complement system into transformative medicines, and today it continues to build a diversified pipeline across disease areas with significant unmet need, using an array of innovative modalities. As part of AstraZeneca, Alexion is continually expanding its global geographic footprint to serve more rare disease patients around the world. It is headquartered in Boston, US.

AstraZeneca
AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on social media @AstraZeneca.

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

References

1. Desport E, et al. AL Amyloidosis. *Orphanet J Rare Dis*. 2012;7(54).
2. Grogan M, et al. Light-chain cardiac amyloidosis: strategies to promote early diagnosis and cardiac response. *Heart*. 2017;103:1065-1072.
3. Mollee P, et al. How to diagnose amyloidosis. *Internal Medicine Journal*. 2014;44:7-17.
4. Wechalekar AD, et al. AL Amyloidosis for Cardiologists; Awareness, Diagnosis, and Future Prospects. *JACC: CardioOncology.* 2022;4(4): 427- 441.
5. Kumar N, et al. Global epidemiology of amyloid light-chain amyloidosis. *Orphanet J Rare Dis*. 2022;17(278).
6. ClinicalTrials.gov. A Study to Evaluate the Efficacy and Safety of CAEL-101 in Patients With Mayo Stage IIIa AL Amyloidosis (CARES). NCT Identifier: NCT04512235. Available here. Accessed June 2025.
7. ClinicalTrials.gov. A Study to Evaluate the Efficacy and Safety of CAEL-101 in Patients With Mayo Stage IIIb AL Amyloidosis (CARES). NCT Identifier: NCT04504825. Available here. Accessed June 2025.

Matthew Bowden
Company Secretary
AstraZeneca PLC