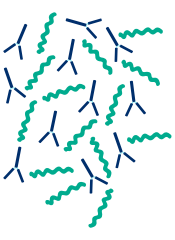
AL Amyloidosis

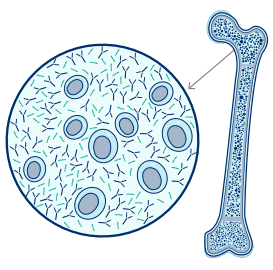
ALEXION®
AstraZeneca Rare Disease

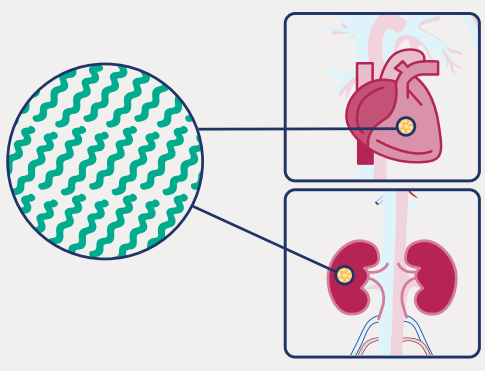
WHAT IS AL AMYLOIDOSIS?



Amyloidosis is a **group of rare diseases** caused by **abnormal proteins that misfold and clump together to form toxic amyloids,** and deposit in tissues or organs.[1]

One type is amyloid light chain, or AL, amyloidosis **where proteins that function as antibodies, also known as immunoglobulins, are produced abnormally by defective plasma cells in the bone marrow.**[1]





Amyloid can buildup in many organs, particularly in the heart and kidneys, which can result in **significant organ damage and organ failure that can ultimately be fatal.**[2]

SYMPTOMS MAY INCLUDE:[3]

Swollen arms and legs

Extreme shortness of breath

Abnormal heartbeat

Nausea

Diarrhea

Numbness or tingling in extremities

Enlarged tongue

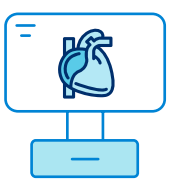
Rash around eyes

and many other **vague symptoms that mimic other diseases** that often complicate diagnosis.[2]

HOW IS AL AMYLOIDOSIS DIAGNOSED?

Diagnosis of AL amyloidosis can be relatively straightforward, but is often delayed and can take **>6 months after symptoms begin.**[4]

Once suspected, blood and urine tests are conducted first, followed by a tissue biopsy to confirm amyloidosis.[5]

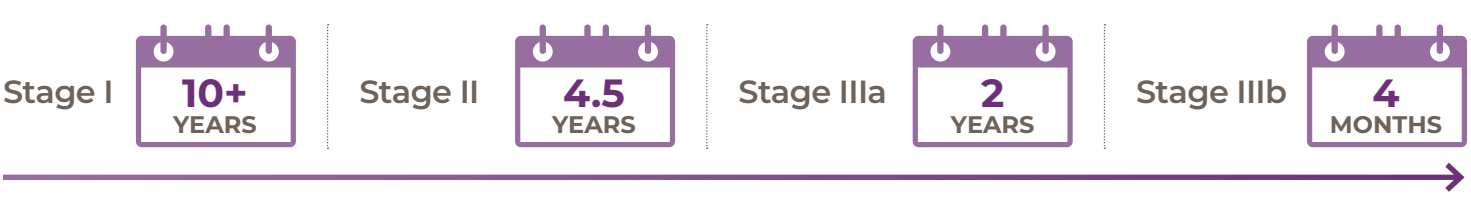


Imaging of the impacted organs can help determine the severity of the condition.[5]

CARDIAC STAGING AND PROGNOSIS

Stage of disease and prognosis mainly depend on the **extent of cardiac involvement and are based on blood tests.**[1]

Median Overall Survival:[5*]



**Based on the 2013 European Modification of the 2004 Standard Mayo Clinic Staging*

Rapid, accurate diagnosis leading to initiation of treatment is essential to mitigate the impact of this disease on **survival and quality of life.**[2]

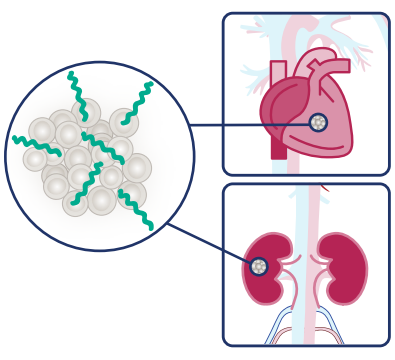
WHAT ARE CURRENT TREATMENT NEEDS?

There are no approved treatments that address the significant organ damage caused by the disease. Current treatments, including **bone marrow transplantation and/or chemotherapy,** focus on preventing and/or suppressing the formation of new toxic amyloids.[1]

As a result, the disease and organ damage may continue to progress and ultimately lead to organ failure and death.[1,6]

WHAT TREATMENT APPROACH IS BEING STUDIED BY ALEXION?

Alexion is advancing the **first potential treatment to address the devastating organ damage caused by AL amyloidosis.**



CAEL-101 is a novel, investigational, **first-in-class therapy** designed to recognize, bind to and remove existing amyloid deposits from organs and thereby improve and/or restore functionality of damaged organs, enhance quality of life and ultimately improve survival.

CARDIAC AMYLOID REACHING FOR EXTENDED SURVIVAL (CARES) CLINICAL TRIAL PROGRAM IN AL AMYLOIDOSIS[7,8]

TRIAL DESIGN

Two parallel, double-blind, randomized **Phase 3 studies** are being conducted to evaluate the efficacy and safety of CAEL-101 combined with current treatments for AL amyloidosis. These studies include patients who are newly diagnosed and have not yet started treatment.

ENROLLMENT

~260 patients with Mayo stage IIIa disease

~110 patients with Mayo stage IIIb disease

70+ study locations across North America, the United Kingdom, Europe, Israel, Japan, and Australia

PRIMARY ENDPOINTS

- Overall survival
- Safety and tolerability

SECONDARY ENDPOINTS

- Improvement in the six-minute walk test
- Quality of life measures
- Improvement in cardiac function

CAEL-101 has received Orphan Drug Designation for the treatment of AL amyloidosis in the U.S. and EU

CAEL-101 is not approved for the treatment of AL amyloidosis. The safety and efficacy of CAEL-101 for the treatment of AL amyloidosis is currently being studied.

References:

1. Desport, E., Bridoux, F., Sirac, C. et al. AL Amyloidosis. Orphanet J Rare Dis 7, 54 (2012).
2. Sanchorawala, V. Light-Chain (AL) Amyloidosis: Diagnosis and Treatment. *Clin J Am Soc Nephrol 1*: 1331–1341, 2006.
3. Amyloidosis - Symptoms and causes. (2020, March 14). Mayo Clinic. Accessed at: https://www.mayoclinic.org/diseases-conditions/amyloidosis/symptoms-causes/syc-20353178. Accessed March 2021.
4. Lousada, I., Comenzo,. Landau, H., Guthrie, S., Merlini, G. Light Chain Amyloidosis: Patient Experience Survey from the Amyloidosis Research Consortium. *Adv Ther* (2015) 32:920–928.
5. Dittrich T., Kimmich C., Hegenbart U., Schönland S., O. Prognosis and Staging of AL Amyloidosis. *Acta Haematol* 2020;143:388-400.
6. Grogan, M., Dispenzieri, A., Gertz, M. Light-chain cardiac amyloidosis: strategies to promote early diagnosis and cardiac response. Heart 2017;103:1065–1072.
7. NIH, U.S. National Library of Medicine. A Study to Evaluate the Effectiveness and Safety of CAEL-101 in Patients With Mayo Stage IIIb AL Amyloidosis. Accessed at: https://www.clinicaltrials.gov/ct2/show/NCT04504825?term=Caelum&cond=AL+Amyloidosis&draw=2&rank=2. Accessed March 2021.
8. NIH, U.S. National Library of Medicine. A Study to Evaluate the Effectiveness and Safety of CAEL-101 in Patients With Mayo Stage IIIa AL Amyloidosis. Accessed at: https://www.clinicaltrials.gov/ct2/show/NCT04512235?term=Caelum&cond=AL+Amyloidosis&draw=2&rank=1. Accessed March 2021.