

TREATMENT OVERVIEW

LIGHT CHAIN AMYLOIDOSIS (AL AMYLOIDOSIS)



*Alison has
AL amyloidosis.*



Amyloidosis
Research
Consortium

ARCI.ORG

KNOWLEDGE IS POWER

ABOUT THE AMYLOIDOSIS RESEARCH CONSORTIUM

The Amyloidosis Research Consortium (ARC) is a nonprofit organization dedicated to driving advances in the awareness, science, and treatment of amyloid diseases. ARC's mission is to improve and extend the lives of those with amyloidosis. ARC is committed to collaborative efforts that accelerate the pace of discovery, expand patient access to the most effective care, and improve short- and long-term outcomes. Working with partners in industry, government, and academia, ARC seeks to spark innovation and to bring promising treatments from labs to clinics. Our outreach and educational efforts inform and empower patients, families, caregivers, physicians, and researchers.

To learn more about ARC, visit www.arci.org or call **(617) 467-5170**.



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INTRODUCTION

AL amyloidosis is a serious disease that is progressive and fatal if left untreated. However, many patients benefit from current therapies, with their lives improved and prolonged, often for many years.

The optimal management of the disease requires early diagnosis, accurate identification of the type of amyloidosis, and effective treatment. Supportive therapies and careful follow-up are also essential.

It is important to learn as much as possible about the disease, its treatment, and how it might affect you. A well-informed patient is better able to be an active partner with their health care team in making decisions about treatment, managing their care, and advocating for their needs.

This booklet is here to serve as a comprehensive resource and a guide for making informed treatment decisions.

AL AMYLOIDOSIS OVERVIEW

Light chain amyloidosis (AL amyloidosis) is a rare systemic disease caused by abnormal blood cells formed in bone marrow. It usually affects people between the ages of 50 to 80 but has also been diagnosed in individuals as young as their 20s. AL amyloidosis affects both men and women, although there is a slight predominance in males. In AL amyloidosis, abnormal plasma cells produce abnormal light chains, these proteins then misfold into amyloid fibers (fibrils). These cause damage by clumping together and accumulating in organs, nerves, and tissues. The pattern of amyloid build-up is different for each patient and often affects more than one organ. Early diagnosis and treatment are essential to prevent or slow disease progression.

In AL amyloidosis, abnormal plasma cells produce abnormal light chain proteins that misfold into amyloid fibrils and accumulate in tissues and organs.

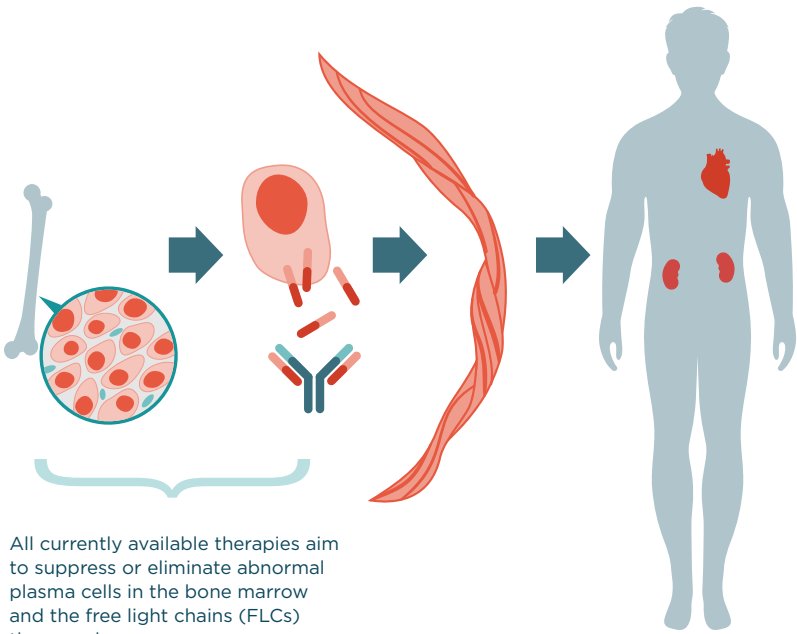
GOALS OF TREATMENT

All currently available therapies aim to suppress or eliminate abnormal plasma cells in the bone marrow and the free light chains (FLCs) they produce. Supportive care is used to manage the symptoms and complications of AL amyloidosis, and to minimize side effects of treatment.

When the rate of free light chain production is slowed or stopped, amyloid buildup declines or halts, and organ function stabilizes or improves.

If treatment stops working or a relapse occurs, a variety of treatment regimens can be used to attack the disease. Multiple therapeutic options are available for all patients, including those with advanced disease at diagnosis.

TREATMENT TARGET



All currently available therapies aim to suppress or eliminate abnormal plasma cells in the bone marrow and the free light chains (FLCs) they produce.

HOW ARE TREATMENT PLANS DECIDED ON?

AL amyloidosis affects each patient in unique ways and requires treatment tailored to each individual. Medical decisions are based on the patient's condition and the risks and benefits of each treatment strategy. Factors considered include patient preference, age, disease progression, which organs are affected, comorbid diseases, and general health.

WHO WILL BE INVOLVED IN MY TREATMENT?

AL amyloidosis is a complex disease best managed by a multidisciplinary team that includes experts in hematology, cardiology, nephrology, neurology, and gastroenterology. Your hematologist will usually lead the team, but collaboration between specialists is crucial to optimize care.

WHAT DO THESE SPECIALISTS DO?

Cardiologist: A doctor who specializes in the heart.

Gastroenterologist: A doctor who specializes in the gastrointestinal tract.

Hematologist: A doctor who specializes in blood disorders.

Nephrologist: A doctor who specializes in the kidneys.

Neurologist: A doctor who specializes in the nerves.

TREATMENTS FOR AL AMYLOIDOSIS

AL amyloidosis and multiple myeloma are both caused by abnormal plasma cells, and treatment regimens for AL amyloidosis have been adapted from those used for multiple myeloma. These include anticancer drugs (also known as cytotoxic drugs) & autologous stem cell transplantation (ASCT).

Your hematologist will create a treatment plan. Most patients take one or two anticancer drugs plus steroid medications. The drugs work together to destroy the plasma cells that make amyloid-producing light chain proteins.

In making treatment decisions, doctors will work to balance the need for a fast response that stops organ damage while minimizing illness due to side effects.

Anticancer drugs are administered in cycles, a dose or a few days or weeks of treatment, followed by several days or weeks without it. The gaps in doses allow healthy cells time to recover before the next cycle.

Many patients respond well after just a few cycles. Lab tests can sometimes show hematologic improvement even earlier. Treatment response is assessed after three cycles and modified as needed.

ANTICANCER DRUGS

Chemotherapy Drugs:

- Melphalan (Alkeran®)
- Cyclophosphamide (Cytoxan®)
- Bortezomib (Velcade®)
- Lenalidomide (Revlimid®)

Immunomodulators:

- Thalidomide (Thalomid®)
- Pomalidomide (Pomalyst®)

Targeted Therapy Drugs:

- Ixazomib (Ninlaro®)

Monoclonal Antibody Drugs:

- Isatuximab (Sarclisa®)
- Daratumumab (Darzalex®)

STEROID MEDICATIONS

- Dexamethasone
- Prednisone

TREATMENT REGIMENS

There are many combinations of anticancer drugs and steroid medications that can be used to treat AL amyloidosis and no one regimen will work for all patients. Your doctor will recommend the best regimen for you based on a number of different factors.

HOW DO ANTICANCER DRUGS WORK?

Anticancer drugs work by damaging or destroying abnormal plasma cells. By stopping their division and reproduction, they prevent the production of amyloid. Some drugs are given by mouth (tablets), while others are administered intravenously (into a vein).

The drugs attack all rapidly dividing cells in the body. This includes abnormal plasma cells, but may also include others, such as hair follicles and cells that line the mouth and stomach. This is what causes side effects during treatment.

HOW DO STEROIDS WORK?

Steroids are hormonal substances naturally produced in the body. Those used to treat AL amyloidosis suppress inflammation and immune function. They are known as glucocorticoids. When used with chemotherapy, they boost response to treatment over what is seen when chemotherapy is used alone.

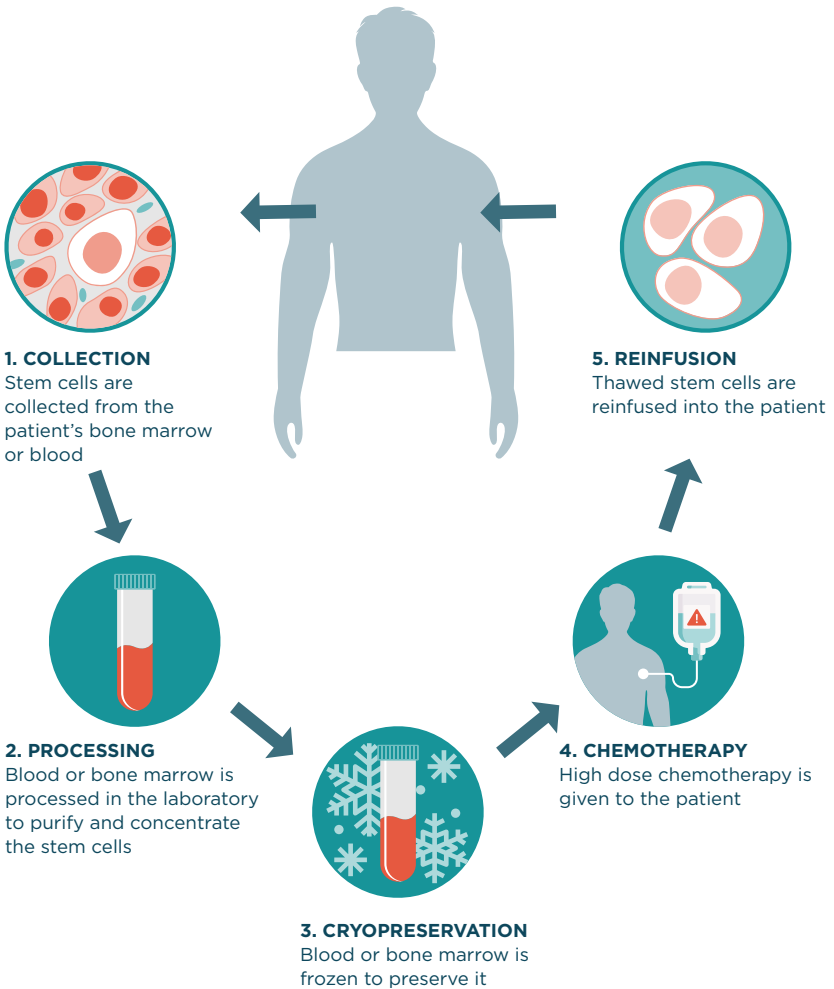
WHAT IS AN AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT)?

ASCT is an intensive treatment that collects a patient's own stem cells, freezes them for storage, and returns them after high-dose chemotherapy. Chemotherapy, a type of anticancer drug, is used to eliminate, kill, shrink, or inhibit the growth of abnormal cells.

High-dose chemotherapy wipes out all blood-forming stem cells made in the bone marrow. After high dose chemotherapy, the patient's own stem cells are reinfused to "rescue" the bone marrow and make it grow new cells. To avoid the risk of life-threatening complications, only those at low risk are eligible for ASCT, or some 20% of patients with AL amyloidosis. Patients are screened based on age, organ involvement, comorbid conditions, and eligibility is determined on a case-by-case basis.

You can inquire with your treatment center about how many patients with AL amyloidosis (not myeloma) have received a stem cell transplant from their care team.

AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT)



WHAT HAPPENS DURING A STEM CELL TRANSPLANT?

COLLECTION

Stem cells are collected (or harvested) prior to high dose chemotherapy. This is done by apheresis, a procedure in which blood is drawn into a machine that separates and collects the stem cells while returning the remaining blood components back into the patient's bloodstream.

TRANSPLANTATION

Collected stem cells are frozen and stored. After high dose chemotherapy, the stem cells are returned to the patient in a way that is similar to a blood transfusion.

RECOVERY

Bone marrow recovery (also called engraftment) takes about two weeks. You may receive blood and platelet transfusions, and antibiotics to prevent infection.

The recovery process takes several months. Depending on where your procedure is performed, it may require an inpatient stay until your blood counts return to normal. This is done to help prevent infection.

SIDE EFFECTS OF TREATMENT

Drugs used to treat AL amyloidosis can have many possible side effects, ranging in severity. In most cases, your doctors and nurses can recommend simple measures or medications to help manage them. Sometimes treatment plans are adjusted to reduce side effects.

Many treatment effects are dose-dependent, and improve when the dose is reduced, or the drug is stopped. If one drug needs to be discontinued, an alternative is usually available.

If you experience any side effects, it is important to tell your health care team; some symptoms need to be carefully monitored. Let your doctors know all medications you take, including supplements and homeopathic remedies, as interactions with chemotherapy drugs can have unintended consequences.

Most patients experience some side effects. Usually, simple measures or medications can help manage them.

COMMON SIDE EFFECTS OF TREATMENT

Common side effects of anticancer drugs include nausea and vomiting, diarrhea, infections, mouth sores, hair loss, and fatigue. These drugs can also cause infertility. If this is a concern for you, speak with your doctor about it before starting any treatments and ask what options are available to address this. Depending on which drugs you receive, other side effects can occur, such as peripheral neuropathy or blood clots.

Steroids can cause stomach pain, increased blood sugar, increased risk of infection, increased appetite, mood changes, insomnia, and muscle weakness. Patients with AL amyloidosis often experience swelling (edema) in their legs or feet. This is closely monitored and treated with diuretics, medications that drain excess fluid.

Most side effects are short-term. They can be managed with supportive treatments, and gradually disappear once treatment ends. The time it takes for this to happen varies for each patient.

HOW LONG WILL I NEED ANTICANCER DRUGS?

Regimens involving anticancer drugs are administered in a several-week cycle. Many patients can achieve a good response after just a few cycles of anticancer drugs. Sometimes, lab tests show improvement even sooner. Some regimens may be administered over months or years, depending on the drug and

your body's response to it.

It is important to keep all follow-up appointments so your health care team can monitor treatment outcomes and make any needed adjustments. Early measurement of your response is essential and can have a major impact on your overall progress and outcomes.

SUPPORTIVE CARE

Supportive care is provided to manage the complications of AL amyloidosis as well any side effects from treatment. These therapies include anti-emetics to prevent nausea and vomiting, diuretics, antacid pills to protect the stomach, anti-viral pills to protect against shingles, nutritional assessments, and antibiotics.

For patients with heart and kidney involvement, diuretics are the mainstay treatment. Salt restriction and careful management of fluid balance are important to preserve organ function and quality of life.

HOW WILL I KNOW IF I'M GETTING BETTER?

For you and your loved ones, the most important sign that treatment is working is when you start to feel better. Side effects from chemotherapy may delay relief, but as organ function improves, symptoms and side effects will likely improve as well.

Today's treatments are more effective and less toxic than those used to treat AL amyloidosis just a few years ago. New therapies and improved management of complications can improve quality of life and prolong it for many years after diagnosis.

HOW IS TREATMENT RESPONSE ASSESSED?

Treatment response is assessed in two ways: the effect on your blood (hematological response) and on organ function. It is important to note that organ function may take 6-12 months AFTER hematologic response to improve, so don't be discouraged if you aren't feeling better right away.

HEMATOLOGICAL RESPONSE

There are three tests used to determine hematologic response:

1. Serum free light chain ratio - Everybody has light chains in their blood called kappa and lambda. This test measures the ratio of the two light chains to see if one is “dominating” and making amyloid fibrils. When the ratio is normal, that is a good sign. This test does not differentiate normal light chains from the abnormal light chains.
2. Serum immunofixation electrophoresis testing - this test looks specifically for the abnormal light chain or light chain clones (either kappa or lambda) in the blood.
3. Urine immunofixation electrophoresis testing - this test looks for the bad light chain or clones in the urine.

Serum free light chains are amyloid precursor proteins. They circulate in the bloodstream until they deposit in organs as amyloid fibrils.

LEVELS OF HEMATOLOGICAL RESPONSE		
Complete response (CR)	Very good partial response (VGPR)	Partial response (PR)
Normal FLC ratio (kappa:lambda) and negative urine and serum immunofixation testing	dFLC under 40 mg/L	50% reduction of dFLC from baseline

Regular FLC tests are used to track chemotherapy response. The most useful test is the dFLC (difference between involved and uninvolved FLCs). dFLC is calculated by subtracting the concentration of the normal (uninvolved) light chain type from the concentration of the abnormal (involved) light chain type.

The goal of chemotherapy is to achieve a complete response (CR) or very good partial response (VGPR). If you have a partial response (PR), your doctors may consider a change in your treatment regimen.

ORGAN RESPONSE CRITERIA

NT-proBNP, BNP and troponins are biomarkers of cardiac function that are released in response to changes in pressure inside the heart. A decline in these values is a positive sign.

Kidney function change is measured by levels of excess proteins in the urine (proteinuria). A decrease in this value indicates a good response. Kidney function is also measured by a blood test called creatinine. If this level is high before treatment, a decrease in this level is a good sign. If it is normal, then no change is also a good sign.

Alkaline phosphatase is an enzyme that plays a key role in liver function. A decline in this value and an ultrasound or physical

exam with liver measurement that shows a reduction in liver size are positive signs and are also used to evaluate treatment response.

ORGAN RESPONSE CRITERIA	
NT-proBNP	At least a 30% decrease from a baseline value
Proteinuria	A reduction of 50% or more without an increase in serum creatinine of 25% over baseline
Alkaline phosphatase	A 50% decrease from abnormal values
Abdominal ultrasound (liver)	A decrease in size of at least 2 cm

RELAPSED/REFRACTORY AND YOUR OPTIONS

If your AL amyloidosis stops responding to initial treatment, the disease is referred to as refractory. If it returns after a period of remission, this is called a relapse.

Finding out that your disease is refractory or has relapsed can be stressful and disappointing. Talking about how you feel with your doctor, family, or other patients can help. ARC can offer support and resources to help you during this time and throughout treatment.

Therapeutic options are available if your disease relapses or is refractory. Previous treatments may be repeated if you had a good response to it, or a different regimen may be prescribed. Each patient's situation is unique and is assessed by doctors on a case-by-case basis.

Treatment options are available in the event of relapse or lack of response to treatment. Each patient's situation is unique and is assessed on a case-by-case basis.

ARE OTHER KINDS OF TREATMENT AVAILABLE?

Some patients with AL amyloidosis may be eligible for a heart or kidney transplant if they are in a CR or VGPR. Those most likely to be considered are under age 60 for heart transplant and under age 70 for kidney transplant. Many patients are considered too high-risk due to age, advanced disease, or poor health.

CLINICAL TRIALS

Clinical trials are investigational studies that aim to prove the efficacy and safety of new treatments. Any drug or therapy for any disease that is approved today is made available because of clinical trials and the participation of patients in those trials.

Trials may test whether new drugs or new combinations of current treatments are better than the currently available standard care. Those who enroll in clinical trials could be the first to benefit from advances in care, but there could also be some unexpected side effects or risks. It's important you talk to your healthcare team about what's involved in a clinical trial so you can make an informed decision about your participation.

Some benefits to participating in a clinical trial may include:

- Benefitting from the latest advances in research and new treatments
- More frequent testing and monitoring from disease specialists
- Helping researchers learn and improve on treatments for years to come

Some potential risks associated with clinical trial participation may include:

- Unexpected side effects
- New treatment might not work as expected
- You may be in a “control” group that gets the standard care and not the new treatment

ARC is here to help you find clinical trials and treatment centers staffed with experts who specialize in the care of patients with AL amyloidosis.

FUTURE DIRECTIONS

Treatments for AL amyloidosis have markedly improved over time, and continue to do so, with clinical trials underway on therapeutic strategies, novel drugs, and immunotherapies.

While early identification and aggressive treatment remain the only ways to achieve complete remission and organ response, the prognosis for those with AL amyloidosis has improved greatly in just a short period of time. The months and years ahead hold great promise for extending and improving the lives of all patients with AL amyloidosis.

QUESTIONS FOR YOUR MEDICAL TEAM

Before undergoing treatment for AL amyloidosis, you will want to make sure that all your questions, concerns, and needs are addressed. Here are some questions you should consider asking your care team.

- What treatment options do I have available? What are the risks and benefits of each?
- How will treatment affect my normal routine? How will I feel before, during, and after this treatment?
- Has this treatment been successful for others?
- What lab values and test results are important to monitor response and side effects?
- Is there a clinical trial that might be better suited to treat my disease?
- What resources are available for me and my family?
- What should I do to prepare for treatment?
- Who will oversee my care and what's the best way to get in touch if there are questions or emergencies?

POST-TREATMENT

- How often will I need blood tests and other follow-up care?
- Will I need other medications or treatments?
- How will I know if the AL amyloidosis has come back?

MAP | My Amyloidosis Pathfinder

New trials are always in development to help expand treatment options and improve quality of life. Join MAP to receive notifications as new clinical trials and treatment centers are posted.



Treatment
Center
Selector



Clinical Trial
Finder

www.myamyloidosispathfinder.org

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- » *Alexion Pharmaceuticals*
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GLOSSARY

AL amyloidosis. A progressive form of systemic amyloidosis caused by abnormal plasma cells that produce light chain proteins; these misfold into amyloid and circulate in the blood, building up deposits in multiple organs and tissues.

Antibodies. Proteins in the blood produced by specialized white blood cells (plasma cells) that fight infection and disease; also called immunoglobulin.

Apheresis. A procedure that draws blood into a machine that separates and collects stem cells and returns the rest of the blood components to the donor or patient.

Autologous stem cell transplant (ASCT). A procedure in which a patient's own stem cells are collected, stored, and then given back following high-dose chemotherapy.

Blood count. The number of red cells, white cells, and platelets in the blood.

Chemotherapy. Treatment with powerful drugs intended to kill cancer cells and cancer-like cells. Chemotherapy may be intravenous (administered through a vein) or oral (in pill form).

Clinical trial. A research study of the safety and effectiveness of new or existing treatments in patients who have provided informed consent and understand potential risks and benefits. Trials are carried out after positive results in laboratory experiments, with the goal of finding better ways to prevent, detect, diagnose, or treat a disease.

Creatinine. A product of energy metabolism normally filtered out of the blood and found in urine; elevated levels in the blood can indicate impaired kidney function.

Edema. Swelling, particularly in the feet and legs, due to fluid retention.

Fatigue. Feeling extremely tired, exhausted, or lethargic all or most of the time.

Free light chain (FLC). Part of an immunoglobulin (antibody) that circulates freely in the bloodstream.

Immune system. The complex group of cells and organs that protect the body against infection or disease.

Immunoglobulins (Ig). A protein that helps protect the body from infection; also called an antibody.

Immunomodulatory drugs. A drug that acts on the cells involved in the body's immune system.

NT-proBNP. N-terminal pro-brain natriuretic peptide; a biomarker of cardiac function.

Plasma cells. Specialized white blood cells that produce immunoglobulins (antibodies) to fight infection; in AL amyloidosis, these cells produce toxic light chain fragments that misfold into circulating amyloid.

Prognosis. The probable outcome or course of a disease.

Proteasome inhibitor. A drug that interferes with the normal functioning of part of a cell called the proteasome, causing abnormal cells to die while leaving healthy cells less affected.

Quality of life. A term that refers to a person's level of comfort, enjoyment, and ability to engage in daily activities. It is a measure of overall well-being.

Refractory. AL amyloidosis that has failed to respond to previous treatment.

Relapse. AL amyloidosis that responded to a previous treatment but shows signs of returning.

Serum Free Light Chain Assay. A blood test used to measure the amount of free light chains in the blood.

Side effects. Any undesired actions or effects of a drug or treatment.

Stem cells. The cells from which blood cells develop; normally found in the bone marrow.

Steroid. Hormonal substances naturally produced by the body; used to suppress inflammation.

Ultrasound. A medical test that uses high-frequency sound waves to capture live images from the inside of your body; also known as sonography.

White blood cell. A major cell type produced in bone marrow that attacks infection and cancer cells; they are part of the immune system.

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