DISEASE AND TREATMENT OVERVIEW

WILD-TYPE TRANSTHYRETIN AMYLOIDOSIS

James has wild-type 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 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**.

Amyloidosis Research Consortium

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This booklet is not intended to provide medical advice. It is merely an educational tool. Patients should speak with their care team when making any treatment decisions

INTRODUCTION

Wild-type transthyretin amyloidosis (ATTRwt) is an age-related disease caused by **transthyretin (TTR)** proteins that become unstable, misfold, and build up in organs and tissues, impairing their function. It is a slowly progressive condition that affects older people, most often Caucasian men over 65 years of age. Heart disease is the hallmark of ATTRwt, but it is commonly preceded by other conditions, such as carpal tunnel syndrome or spinal stenosis.

Until 2014, ATTRwt was known as *senile systemic amyloidosis.* There were no approved treatments until recently. Advances in imaging technology and the development of new drugs are improving how the condition is diagnosed and treated.

WHAT IS AMYLOIDOSIS?

Amyloidosis is a group of diseases caused when misfolded proteins, called amyloid, build up and form fibrils that deposit in the body's organs and tissues, affecting their ability to function. Amyloid fibrils typically accumulate in the heart, kidney, gastrointestinal tract, and nerves; less often in the liver, spleen, and airway. These can impair multiple organs and nerves or be localized in one area of the body. Symptoms are often mistaken for more common conditions.

Over 30 different proteins can cause amyloidosis. Each protein has different associated symptoms and treatments and is linked with a unique sub-type of amyloidosis. Each sub-type is referred to by an "A" for amyloid, followed by an abbreviation for the abnormal protein. For example, AL amyloidosis is caused by abnormal **immunoglobulin Light chains**, and ATTR is caused by abnormal **transthyretin (TTR)** protein. Treatment is determined by the type of amyloid and which organs and tissues are affected.

Amyloid is a starch-like substance caused by the misfolding of proteins. Amyloid bind together into rigid fibrils that accumulate in tissues and organs.

WHY ARE PROTEINS SO IMPORTANT?

Many thousands of proteins do essential work inside our cells. Each has a specific job to keep us healthy. DNA instructions control the shape and structure of proteins. Normal proteins form (fold) into a specific shape, do their tasks, and are then recycled or removed from the body.

In amyloidosis, mutated proteins form incorrectly (misfold), which makes them unable to do their tasks and difficult for the body to remove. These misfolded proteins then accumulate in the body and form fibrils, known as amyloid, in organs and tissues, such as the heart, kidney, or nerves. As they accumulate over time, they impact the function of organs, causing symptoms to flare, which tells us something is wrong.

Many different proteins can misfold and lead to different types of amyloidosis, but they all share the same abnormal structure. Diagnostic tests can identify specific types of amyloid.

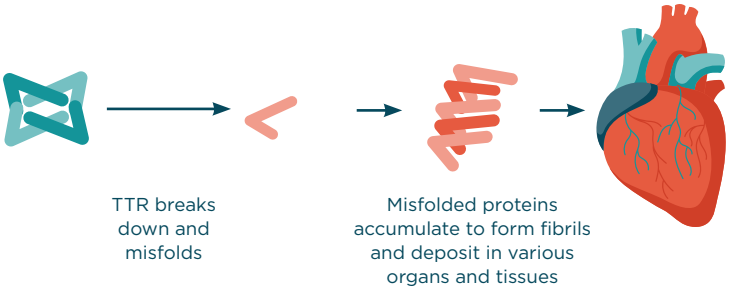
Abnormal transthyretin (TTR) proteins are seen in two types of amyloidosis: hereditary transthyretin amyloidosis (hATTR) and wild type transthyretin amyloidosis (ATTRwt). The natural course of disease for hATTR and ATTRwt differ, making it important to correctly identify the type.

WHAT IS WILD-TYPE TRANSTHYRETIN?

Wild-type transthyretin amyloidosis (ATTRwt) is a progressive disease caused by TTR proteins that become unstable during the aging process and misfold, leading to deposits of amyloid fibrils that build up in organs and tissues. ATTRwt typically affects the heart, with cardiac dysfunction being the primary symptom. Wild-type TTR can also accumulate in soft tissues such as around tendons, wrists, and the spinal column causing carpal tunnel, trigger finger, tendon rupture and spinal stenosis.
(SEE SYMPTOMS).

In wild-type TTR amyloidosis, the transthyretin protein misfolds and is unstable due to factors related to aging. It is not the result of a genetic mutation, as with the hereditary form of ATTR.

BREAKDOWN AND MISFOLDING OF TTR PROTEINS



HOW COMMON IS ATTRwt?

Although there are no exact figures on the **prevalence** of ATTRwt, it's believed to be greatly underdiagnosed. Some experts believe that it is not a rare disease. One estimate found that 10% to 25% of patients with other forms of heart failure had cardiac amyloid deposits. As the population ages, the number of cases of ATTRwt increases, driving efforts to increase awareness of the disease and to develop new therapies to treat it.

SYMPTOMS

Congestive heart failure is the defining sign of ATTRwt. Amyloid fibrils infiltrate the heart muscle, causing it to thicken and become enlarged and stiff. This makes it harder for the left ventricle, the main pumping chamber, to do its job. Although right-sided heart failure is less common, it may also occur. As the heart works to compensate for the effects of the amyloid deposition, symptoms arise, warning us that something is wrong.

Amyloid deposits can also affect other parts of the body, causing polyneuropathy, which is weakness, numbness, or burning pain of peripheral nerves. Bilateral carpal tunnel syndrome, spinal stenosis, trigger finger, and tendon rupture can be early indicators

of ATTRwt, or occur at later stages of the disease. More research is needed to find out how prevalent nerve involvement is in those with wild-type TTR amyloidosis.

HOW DOES ATTRwt AFFECT THE BODY?

The heart

Amyloid deposits can cause **congestive heart failure** (weakness of the heart that leads to a buildup of fluid in the body); hypertrophic cardiomyopathy (thickening of the heart muscle); coronary artery disease; an irregular heartbeat (**arrhythmia**); or syncope (fainting). Symptoms can include nausea, weight loss, shortness of breath, inability to sleep, fatigue, dizziness, and fluid retention or swelling in the feet, legs, or abdomen (edema)..

The muscular and skeletal system

Carpal tunnel syndrome in both wrists may be caused by the deposition of amyloid and can be one of the first symptoms of ATTRwt. This can cause pain, numbness, or tingling in both hands and arms and a weak grip. Other common symptoms include **Lumbar spinal stenosis** (compression of lower back nerves, causing pain, numbness, or weakness in the legs). Spontaneous rupture of bicep tendons is also a symptom.

Carpal tunnel syndrome and spinal stenosis often precede the onset of cardiac symptoms but can recur as the disease progresses.

WHAT ARE OTHER NONSPECIFIC SYMPTOMS?

Nonspecific symptoms are those that can be caused by a wide range of illnesses. Fatigue is one example. Others may include fever, general malaise, weight loss, difficulty concentrating, or stiffness. The onset of ATTRwt amyloidosis is typically slow, occurring over many years. Because the disease is rare, physicians tend to attribute symptoms to other, more common disorders.

DIAGNOSIS

There are several different amyloid proteins that can cause heart failure. Each different type of amyloidosis has a different treatment, clinical course, and prognosis. Therefore, an accurate diagnosis is essential. Every patient with amyloidosis should be told which type they have by their providers.

WHY IT IS IMPORTANT TO KNOW YOUR DISEASE

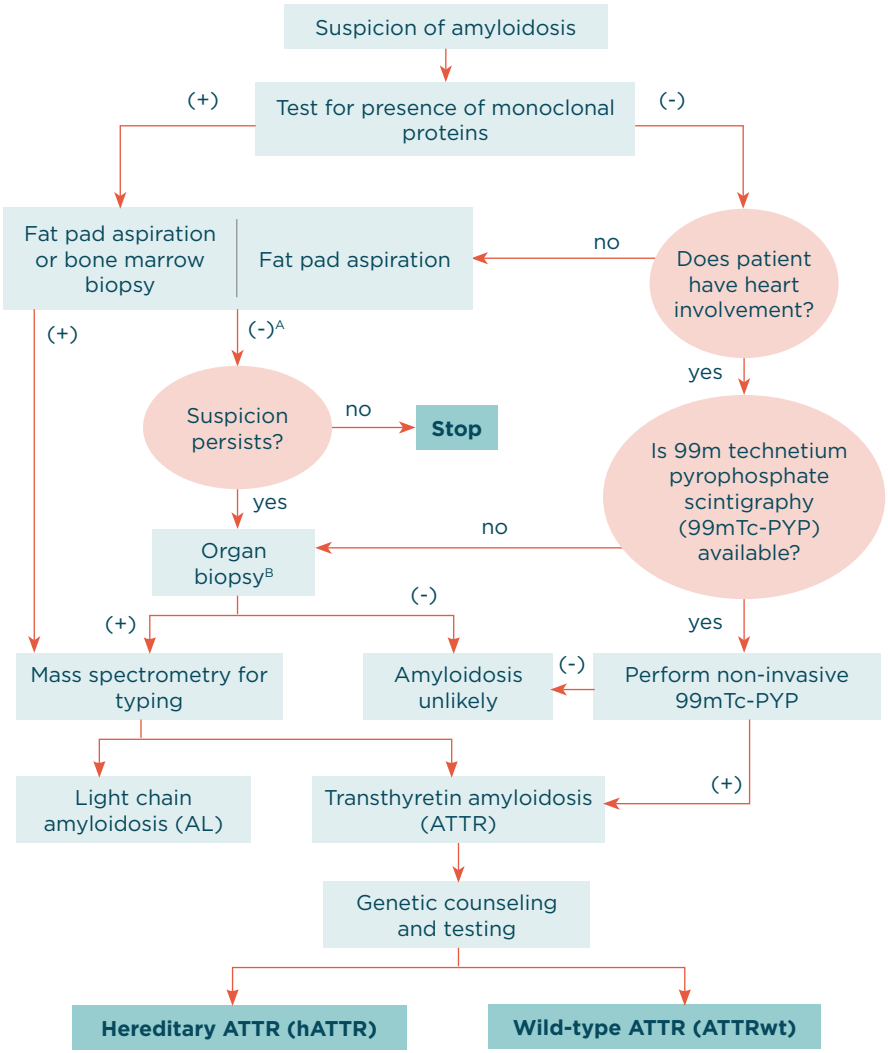
While ATTRwt is not caused by a genetic mutation, it does lend itself to misdiagnoses and delays in getting effective care, commonly also seen in its hereditary counterpart, hATTR. Onset of the disease is gradual, symptoms can be vague, and many older patients have other underlying diseases. Cardiac symptoms also mimic common conditions, such as **congestive heart failure**, in this age group. Your understanding of diagnostic priorities and procedures can help you know what tests to expect and how their outcomes can affect your treatment plan.

DIAGNOSTIC PRIORITIES

Ruling out **immunoglobulin light chain amyloidosis (AL amyloidosis)**, one of the most common forms of systemic amyloidosis, is a critical goal in diagnostic testing. The main treatments for AL amyloidosis, chemotherapy and stem cell transplantation, are radically different from those of TTR amyloidosis.

Biopsy is the gold standard for diagnosing ATTRwt. Usually, a small sample of fat is taken from the patient's lower abdomen to test, but the **biopsy** could also be a sample of skin or heart muscle (**endomyocardial biopsy**). The sample(s) are then stained with Congo red dye and viewed under a microscope with polarized light. Stained amyloid has a characteristic apple-green color or birefringence that identifies it under polarized light. While biopsy is the gold standard, this test is not 100% accurate.

THE DIAGNOSTIC WORKUP



Step in the diagnostic algorithm (test, biopsy, or conclusion)

Key question in determining next step

A A negative fat pad or bone marrow will exclude amyloidosis in 85% of cases. Clinical evidence should be evaluated to determine if there is still suspicion.

B Depending on clinical presentation, appropriate organ biopsy will differ. Common sites are heart, kidney, liver, and nerve.

Once the presence of amyloid is confirmed, the type of amyloid protein needs to then be determined through a process known as **laser microdissection with mass spectrometry**. If this test confirms ATTR, genetic testing is then required to differentiate wild-type ATTR (ATTRwt) from hereditary amyloidosis (hATTR). Differentiating between them is important for making sound personal and medical decisions.

To learn about other types of amyloidosis, see our companion booklets and visit www.arci.org.

Although an endomyocardial biopsy (biopsy of the heart tissue) is still the definitive diagnostic tool, nuclear imaging (scintigraphy) is emerging as a highly accurate, noninvasive option.

MORE ON DIAGNOSITC TESTING

Radionuclide bone scintigraphy (e.g. PYP, technetium scan or DPD scintigraphy)

Nuclear imaging is a recent innovation in the diagnosis of wild-type ATTR. It can distinguish amyloidosis from other conditions that thicken the heart wall and gauge the severity of disease. Scintigraphy is less reliable if a patient has a monoclonal gammopathy or AL amyloidosis.

Electrocardiogram (EKG)

The electrocardiogram (EKG) is the oldest and most widely used test for cardiac dysfunction. It records the electrical activity of the heart, but its use can lead to missed or incorrect diagnoses. ATTRwt looks much like other cardiac conditions on an EKG readout, and subtle differences are frequently misinterpreted. Results from an EKG may create suspicion for ATTRwt, but it should never be used as a definitive diagnostic tool.

Echocardiogram (Echo)

Echocardiograms are also widely used to assess suspected cardiomyopathies such as ATTRwt. It can show changes in the structure and function of the heart, but images can be misread. Echo images of ATTRwt can be mistaken for other forms of amyloidosis or non-amyloid causes of heart failure. Results from an echo can be indicative of amyloidosis but cannot be used alone to diagnose a patient.

Cardiac magnetic resonance imaging (CMR)

A CMR is a noninvasive scan used to create detailed images of the heart at work and can demonstrate amyloid deposition in the heart. It does not identify what kind of amyloid is present and sometimes other types of cardiac disease can look very similar on CMR. Other downsides are cost and possible kidney injury from the dye used. CMR may be helpful in some patients but is not required for a diagnosis.

Endomyocardial biopsy

A **biopsy** of heart muscle tissue is the gold standard for definitive diagnosis of ATTRwt. Samples are stained with a dye called Congo red and then examined under a polarized light microscope. If amyloid is present, it shows a unique apple-green birefringence (refraction). **Mass spectroscopy** is then used to identify the specific protein and type of amyloidosis. This approach delivers diagnostic certainty, but EMB is an invasive procedure with risk of complications. It requires expertise that may not be readily available where you live.

Genetic testing

Once a diagnosis of ATTR is confirmed via **biopsy** or scintigraphy, genetic testing is required to rule out hereditary TTR amyloidosis. Knowing which type of amyloidosis you have is the first step in mounting an effective defense against it.

SHOULD I GET A SECOND OPINION?

Although amyloidosis is a rare disease, clinical expertise has

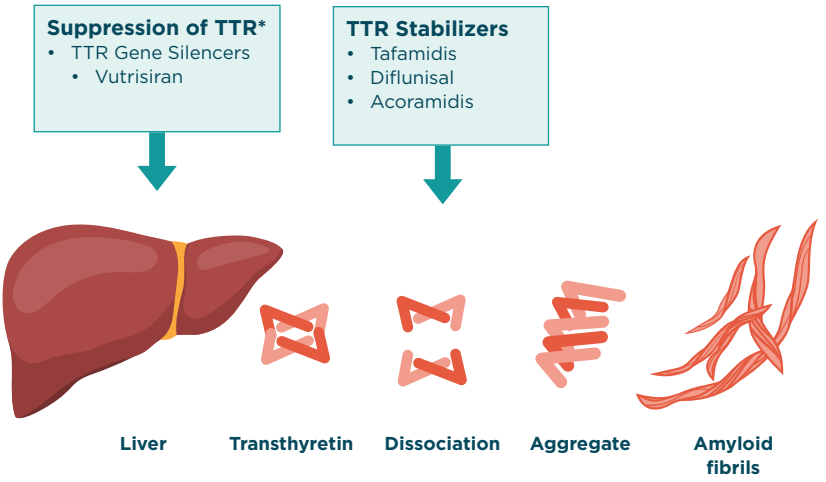
developed and expanded into amyloidosis treatment centers around the U.S. and other parts of the world. Patients seeking a second opinion before starting treatment will find amyloidosis expertise in these treatment centers. Check with your insurance company about coverage of a second opinion.

HOW IS ATTRwt TREATED?

TREATMENT GOALS

The goals of treatment are to manage cardiac dysfunction in ways that reduce the burden of symptoms, and to target the underlying amyloidosis to slow disease progression. Newly available drugs work to disrupt the disease process by stabilizing TTR proteins, slowing its production.

TARGETS OF TREATMENT THROUGH THE DISEASE PROCESS



The more you know about how ATTRwt is diagnosed and treated, the better you'll be able to make informed decisions about your care.

AVAILABLE APPROVED TREATMENTS

TTR Stabilizers

ATTRUBY™ (acoramidis)
Acoramidis is a TTR stabilizer approved for use in the U.S. treating patients with **transthyretin** amyloidosis (ATTR) who have heart involvement (cardiomyopathy). The drug works by binding to the TTR protein and helping to stabilize that protein structure, preventing it from breaking down, misfolding, and forming fibrils.

In the randomized, double-blind, placebo-controlled Phase III ATTRibute-CM clinical trial, acoramidis resulted in a statistically significant better combined outcome that took into account death, hospitalization, biomarker, and function.

Acoramidis is a 712mg tablet taken by mouth twice a day and is generally well tolerated. The most commonly observed side effects were diarrhea and stomach-area (abdominal) pain. These are not all of the possible side effects of Attruby.

BridgeBio (Palo Alto, CA, USA) www.bridgebio.com.

VYNDAMAX® (tafamidis)
Tafamidis is a selective TTR stabilizer approved for use in the U.S. and Canada to treat cardiomyopathy in adults with hereditary TTR amyloidosis (hATTR) and approved for use in Europe, Mexico, Japan, Argentina and other countries to slow the disease progression of polyneuropathy in early stage hereditary TTR amyloidosis (stage I-III). The drug works by binding to TTR protein to prevent misfolding that leads to amyloid fibrils.

In the randomized, phase III ATTR-ACT clinical trial in patients with hATTR-CM, tafamidis significantly reduced all-cause death and heart disease related hospitalizations in patients with early disease. It also slowed loss of function and helped maintain quality of life.

Tafamidis is a 61mg capsule taken by mouth once a day and has very few reported side effects in patients with cardiomyopathy.

Pfizer (New York, NY USA) www.pfizer.com

Gene Silencers

AMVUTTRA® (vutrisiran)
Amvuttra (vutrisiran) is a gene silencer approved for use in the U.S., Canada, Europe and several other countries, for treating patients with hereditary **transthyretin** amyloidosis (hATTR) who have peripheral nerve involvement (polyneuropathy). and/or cardiomyopathy (heart damage). This is another drug using RNA interference (RNAi) to inhibit the production of TTR protein in the liver, reducing TTR levels in the body and preventing amyloid build-up and organ damage.

In the phase III HELIOS-B clinical trial, patients with cardiomyopathy who received Amvuttra had a lower risk of death and heart-related hospital visits compared to those who received the placebo. Patients also maintained better physical function and quality of life. Amvuttra is a subcutaneous (under the skin) injection administered by a health care professional in a hospital or clinic setting once every three months.

Alnylam Pharmaceuticals (Cambridge, MA, USA)
www.amvuttra.com

Organ transplantation

Depending on the damage to the heart or other organs, a heart or other organ transplant may also be considered. Transplantation, though well-established, is costly and high-risk. Post-transplant complications are common. Outcomes depend on age of onset and type of mutation. Other factors include age at the time of transplant and nutritional status. Transplant slows the disease but does not stop it.

Off-label treatments are prescribed by physicians based on expert opinion, small study outcomes, or clinical experience. Because the claims can often be misleading, you should discuss them with your health care provider to find out if they might be right for you.

OFF-LABEL AND OVER THE COUNTER (OTC) TREATMENTS

Off-label drugs means they are used for indications other than what is approved by the FDA. Physicians prescribe them based on expert opinion, small study outcomes, or clinical experience. Some have been on the market for many years but have yet to go through the rigorous testing needed to gain FDA approval for a new use. We recommend that you discuss off-label drugs with your physician to see if they might be right for you.

OTC drugs and supplements are available online or in retail outlets without a prescription. Claims of health benefits may be misleading, so check with your physician before you start taking them.

OFF-LABEL TREATMENTS

DOLOBID® (diflunisal)

Diflunisal is an NSAID (non-steroidal anti-inflammatory drug) that also works as a TTR stabilizer. NSAIDs are common medications to reduce inflammation and diflunisal is also used in patients to decrease arthritis pain. It may be prescribed off-label for treating ATTR polyneuropathy, with limited data in ATTR cardiomyopathy usage.

In a 24-month randomized clinical trial in patients with hATTR-PN, diflunisal slowed progression and preserved quality of life. It also led to a two-to-threefold improvement in neuropathy impairment scores. In a nonrandomized single-center study in patients with

hATTR-CM, it delivered a significant survival benefit.

Diflunisal is a 250mg tablet taken by mouth twice a day and is widely available at low cost. Side effects are kidney disease, gastrointestinal upset or bleeding, and worsening fluid retention thus, it is not suitable for all patients.

Merck and Co., Inc. (Whitehouse Station, NJ USA)
www.merck.com

OVER THE COUNTER (OTC) TREATMENTS

GREEN TEA (EGCG)

Green tea contains Epigallocatechin-3-gallate (EGCG), a well-known major polyphenol which may inhibit formation of TTR amyloid fibrils and help break up amyloid deposits. Two trials that followed patients for 12 months showed that green tea significantly reduced left ventricular mass by up to 13% in patients with ATTRwt. This early evidence suggests that green tea can slow the progression of ATTR cardiomyopathy. The extract from green tea is available in a capsule. More research is needed to confirm the benefits.

INVESTIGATIONAL TREATMENTS

Investigational drugs for ATTRwt are in various stages of clinical trials and research and hold promise for the treatment of patients with ATTRwt. Please see our ARC Talks webinar on Clinical Trials Updates for more up-to-date information.

SYMPTOM MANAGEMENT

SUPPORTIVE CARE

Supportive care to relieve symptoms is the mainstay therapy for ATTRwt. Surgery can ease pain and disability from spinal stenosis or carpal tunnel syndrome and select patients with end-stage disease may qualify for a heart transplant.

Although heart transplant isn't a viable option for most patients

with ATTRwt, medications are routinely used to manage heart failure symptoms and extend survival. These work well, in general, but only a few of these agents can be safely prescribed for those with ATTRwt. Not all physicians are aware of recently identified risks, but it's important that you are. It is also important to note that every patient is different, so medications prescribed for one patient may not be the best option for another. Always consult your physician before starting or stopping any medications.

AN OVERVIEW OF HEART FAILURE DRUGS AND MEDICAL DEVICES

Some common drugs used for other forms of heart failure may cause adverse effects in amyloidosis patients. It's important to be aware of the risks. Always consult your physician before starting or stopping any medications.

Diuretics (water pills): Used to stabilize weight and reduce symptoms by flushing salt and water from the body. Loop diuretics, the strongest kind, are the first line treatment for heart failure, but aggressive use can lead to kidney damage and low blood pressure (hypotension).

ACE inhibitors (angiotensin converting enzyme inhibitors), β-blockers (beta-blockers), and ARBs (angiotensin receptor blockers): Used alone, or in combination, to treat hypertension, control heart rate and rhythm, and manage other kinds of cardiac dysfunction. However, these agents don't slow disease progression or relieve symptoms in patients with ATTRwt. In fact, they may worsen fatigue and hypotension, and should be used cautiously.

Digoxin: Used to slow and strengthen the heartbeat. In patients with ATTRwt, **digoxin** may bind to the amyloid fibrils in the heart and cause toxicity, so this medication is usually avoided. Patients who can tolerate it should be closely monitored.

Calcium channel blockers: Used to control heart rate and blood pressure. There are two types of calcium channel blockers; dihydropyridines (DHPs) and nondihydropyridines (non-DHPs). The DHPs are well tolerated in patients with ATTRwt but the non-DHPs (i.e. verapamil and diltiazem) may bind to amyloid fibrils

and worsen heart failure, therefore are often avoided. A physician will determine if these drugs may be a good option for a patient.

Amiodarone: Used to control heart rhythm and improve symptoms. It's well-tolerated in patients with ATTRwt, with no known adverse effects on blood circulation.

Medical Devices: Patients with ATTRwt tend to be at high risk of arrhythmias and other conduction system abnormalities. Many have **pacemakers** (devices that regulate heartbeat) or defibrillators (devices that shock the heart out of an irregular heartbeat) implanted. Those with end-stage heart failure may qualify for a **left ventricular assist device (LVAD)**. Due to concerns about increased mortality in patients with ATTRwt, LVAD implants are not typically used and are assessed on a case-by-case basis.

ATTRwt cardiomyopathy is increasingly recognized as a unique disease that calls for specialized care. But this knowledge will take time, potentially many years, to be fully embraced by the medical community.

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 upon 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.

Clinical trials can help patients access the newest treatments before they come to market.

ARC PATIENT SUPPORT AND RESOURCES

The Amyloidosis Research Consortium (ARC) is a nonprofit organization with a mission to advance scientific discovery, improve access to state-of-the-art care, and empower patients with innovative educational tools and support. for more information on ATTRwt, visit our website at www.arci.org.

To learn about treatment centers and set up personalized notifications for clinical trials, visit our free online tool, My Amyloidosis Pathfinder:

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

KEY QUESTIONS TO ASK YOUR HEALTH CARE TEAM

Therapeutic education and genetic counseling can answer many questions. Research in medical journals and information from advocacy groups like ARC may answer others. Some common questions about treatment are listed below.

1. Where is the closest specialized amyloidosis treatment center and will you provide a referral?
2. What tests are required before I can begin treatment?
3. What will these tests show and how reliable are they?
4. How will I know if I've had all the necessary testing completed?
5. How will my treatment strategy be determined?
6. Who is on my care team?
    a. What specialists will be involved in my care and why?
    b. Who will be my main point of contact for treatment and care navigation and how do I get in touch with them?
    c. Who will coordinate care and arrange for regular monitoring and follow-up?
7. Am I eligible for treatment with new drugs?
8. Will my treatment be covered under insurance?
    a. Who can I talk to if I have questions about my insurance coverage?
9. What can I expect as we move forward with my treatment plan?
10. What emotional support is available for me and my caregiver(s) as we navigate this diagnosis?

GLOSSARY

Aldosterone antagonists. Diuretic drugs, often used in combination with other drugs, for the management of chronic heart failure.

Amiodarone. An antiarrhythmic medication used to treat and prevent many types of irregular heartbeats.

Amyloid. A starch-like substance caused by the misfolding of proteins. Amyloid binds together into rigid, linear structures (fibrils) that accumulate in tissues and organs.

Amyloid fibril: A rigid stack of amyloid proteins that builds up in the body.

Amyloidosis. A disease caused by the accumulation of abnormally shaped proteins (amyloid proteins) in tissues and organs.

Angiotensin-converting enzyme (ACE) inhibitors. Oral medications that lower blood pressure; used to treat hypertension (high blood pressure), coronary artery disease, and heart failure, and to help manage diabetes and kidney disease.

Angiotensin receptor blockers (ARBs). Medicines that dilate (widen) blood vessels; used to treat high blood pressure (hypertension), heart failure, or kidney disease in people with diabetes.

Arrhythmia. An irregular heart rhythm.

Beta-blockers. A class of drugs prescribed after a heart attack or to treat abnormal heart rhythms (arrhythmias); widely used to treat high blood pressure but are no longer first line therapy for most patients.

Biopsy. A small piece of tissue that is removed and examined under a microscope.

Calcium channel blockers. Medications that cause blood vessels to relax and widen (vasodilate) to improve oxygen supply to the heart and lower blood pressure; some also slow the heart rate.

Carpal tunnel syndrome. A common condition that causes pain, numbness, and tingling in the hand and arm; caused when one of the major nerves to the hand, the median nerve, is squeezed or compressed as it travels through the wrist.

Conduction system of the heart. A group of specialized cardiac muscle cells in the walls of the heart that send signals to the heart muscle that cause it to contract.

Congestive heart failure. A condition in which the heart can't pump enough blood and oxygen to the body's tissues. ATTRwt is most often found in patients with a preserved ejection fraction (HFpEF), a common type of heart failure.

Digoxin. A medication used to treat a certain type of irregular heartbeat that can have an adverse effect on patients with ATTRwt heart failure; it's usually used with other medications.

Diuretics. Medications that help flush excess fluid and sodium from the body; used to treat congestive heart failure, liver disease, and kidney disease.

Echocardiogram. An ultrasound of the heart that shows how well it is working.

Ejection fraction (EF). A measurement, expressed as a percentage, of how much blood the left ventricle pumps with each contraction. A normal EF may be between 50 and 70 percent.

Electrocardiography (EKG). A recording of the heart's electrical activity.

Endomyocardial biopsy (EMB). A surgical procedure to take a small sample of heart muscle tissue for diagnostic testing.
FDA. U.S. Food and Drug Administration.

FDA. U.S. Food and Drug Administration.

Hereditary transthyretin amyloidosis (hATTR). A rare, progressive form of systemic amyloidosis caused by an inherited genetic mutation that causes a buildup of amyloid in multiple organs and tissues.

Immunoglobulin light chain amyloidosis (AL amyloidosis). A common form of systemic amyloidosis, caused by an underlying plasma cell abnormality; abnormal protein fibers are made of components of antibodies called light chains.

Left ventricle of the heart. The main chamber of the heart, responsible for pumping oxygenated blood to tissues all over the body.

Left ventricular assist device (LVAD). A mechanical device implanted inside the chest to help a weakened heart pump blood.

Lumbar spinal stenosis. A common cause of low back, buttock, and leg pain in adults aged 50 years and older. The condition is caused by nerve compression; symptoms may include tingling, numbness, pain, and weakness.

Mass spectroscopy. An analytical laboratory technique to separate the components of a sample by their mass and electrical charge.

Pacemaker. A small device placed under the skin of the chest to help regulate heartbeat.

Preserved ejection fraction (HFpEF). A measure, expressed as a percentage, of how much blood the heart pumps with each beat; preserved ejection fraction is over 50%.

Prevalence. The proportion of a population who have a specific characteristic in a given time period.

Proteins. Large, complex molecules coded by our genes that play a central role in biological processes. The work they do in cells.

Transthyretin. A protein mainly produced in the liver that transports vitamin A (retinol) and a hormone called thyroxine throughout the body.

Wild-type transthyretin amyloidosis (ATTRwt). Acquired amyloidosis with a normal (nonmutated) transthyretin protein; typically causes cardiac dysfunction and is seen in men 60 years or older.

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» *Intellia Therapeutics*
» *Ionis Pharmaceuticals*
» *Pfizer*
» *Protego Biopharma*
» *Prothena Biosciences*
» *Ultromics*

You are not alone — ARC is here to support you every step of the way.

To receive one-on-one guidance, learn more about ARC, or support our mission, contact us:

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Newton, MA 02460

Email: **support@arci.org**
Telephone: **(617) 467-5170**
Mon-Fri 9:00 am-5:00 pm EST

Learn more at **ARCI.ORG**

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