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 the awareness, science, and treatment of amyloid diseases. ARCs 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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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.

This booklet discusses the disease process, its symptoms, and how it is diagnosed and treated. It was designed to serve as a guide for making informed treatment decisions. We encourage you to contact your health care provider if you have specific questions about your diagnosis of ATTRwt or treatment.

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. Over 30 different proteins cause amyloidosis. Each is referred to by an "A" for amyloid followed by an abbreviation for the misfolded protein (for example ATTR is amyloidosis caused by the misfolded TTR protein). Treatment is determined by the type of amyloidosis and which organs and tissues are affected.

WHY ARE PROTEINS SO IMPORTANT?

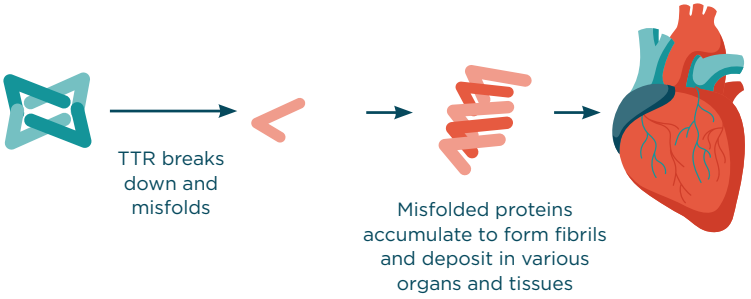
Many thousands of proteins do essential work inside our cells. Each has a specific function to keep us healthy. Normal proteins fold in a specific way, complete their tasks, and are then recycled or removed from the body.

Transthyretin (TTR) is a protein made in the liver that transports thyroid hormone and vitamin A in the blood. The misfolding of TTR leads to amyloid deposits that build up in tissues and organs, causing problems. As amyloid deposits accumulate over time, symptoms flare, telling us something is wrong.

WHAT IS WILD-TYPE TRANSTHYRETIN AMYLOIDOSIS (ATTRwt)?

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.

THE BREAKDOWN AND MISFOLDING OF TTR PROTEIN



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.

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

WHAT ARE THE SYMPTOMS OF ATTRwt?

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, or 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.

COMMON SYMPTOMS OF ATTRwt
Shortness of breath/getting winded
Tiring easily with exercise
Fatigue and/or weakness
Irregular heartbeat or palpitations (arrhythmia)
Fluid retention/swelling in the feet, legs, or abdomen (edema)
Bilateral carpal tunnel syndrome (pain, numbness, or tingling in both hands and arms; weak grip)
Lumbar spinal stenosis (compression of lower back nerves, causing pain, numbness, or weakness in the legs)
Spontaneous rupture of bicep tendons

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

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.

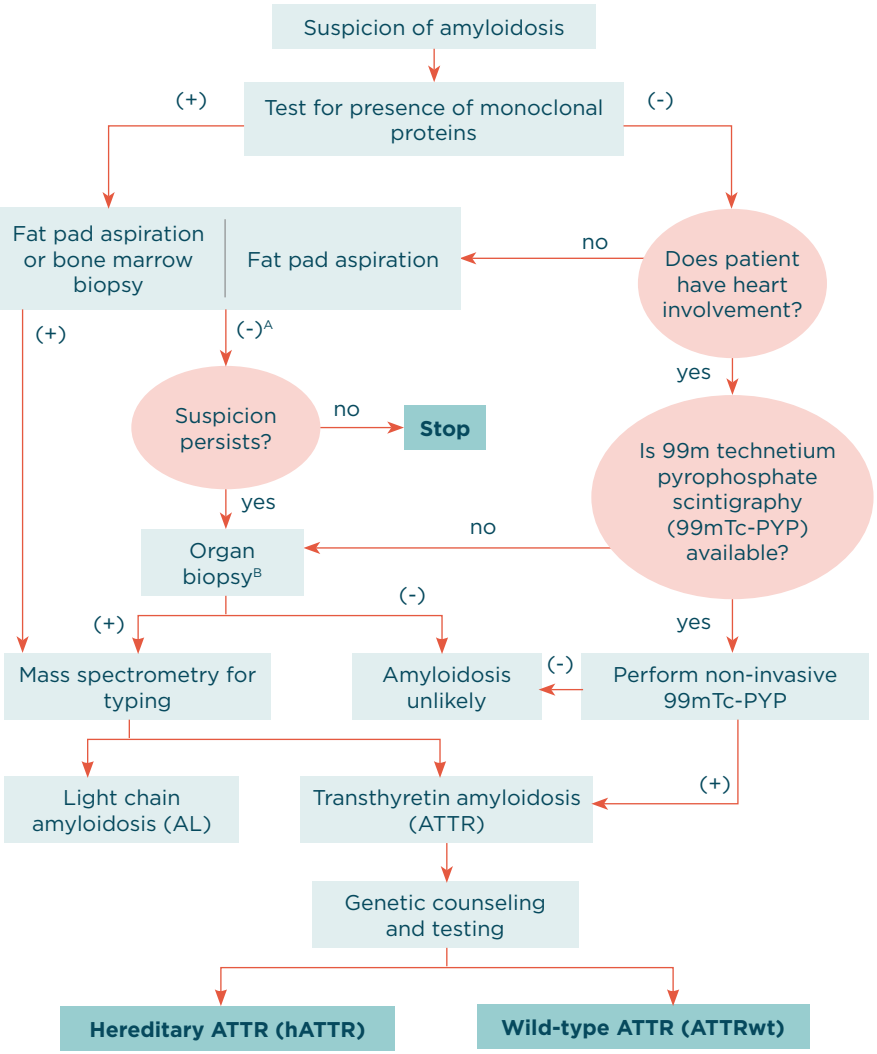
Transthyretin (TTR) is named as such because it transports thyroxine (thyroid hormone) and retinol (vitamin A) in the blood. Transthyretin (TTR) is made in the liver.

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 birefringence," meaning it will appear green under polarized light.

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.

While biopsy is the gold standard, this test is not 100% accurate. 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 tests confirms ATTR, genetic testing is then required to differentiate ATTRwt amyloidosis 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 brochures 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

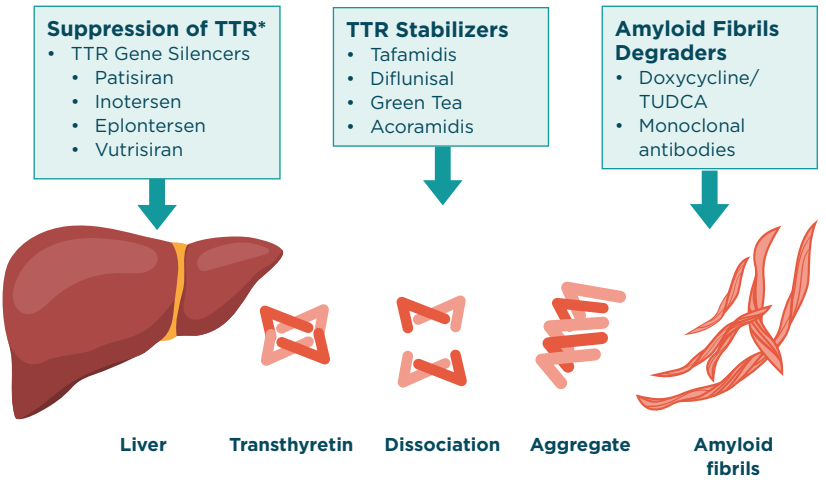
Once a diagnosis of ATTR is confirmed via biopsy or scintigraphy, genetic testing is required to rule out hereditary TTR amyloidosis. Knowing which type of amyloidosis you have is the first step in mounting an effective defense against it.

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



*Gene silencers are not yet approved for use in ATTRwt, only for hereditary. The only treatment currently approved for wild-type is tafamidis.

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

AVAILABLE APPROVED TREATMENTS

Vyndaqel®/Vyndamax® (tafamidis)

VYNDAQEL®/VYNDAMAX® (TAFAMIDIS)		
Current Indications	**How it is administered**	**What are possible side effects?**
Cardiomyopathy in adults with ATTR amyloidosis.	One daily dose of 80 mg taken in four 20 mg capsules; a single 61 mg dose is also available.	• Urinary tract infections • Vaginal infections • Upper abdominal pain • Diarrhea

Vyndaqel®/Vyndamax® is the first disease-modifying drug approved by the FDA to treat cardiomyopathy in adult patients with ATTR. It stabilizes TTR proteins to reduce misfolding and slow the accumulation of amyloid fibrils in organs and tissues.

It comes in 20 mg capsules; the recommended daily dose is 80 mg (four capsules a day). A single-dose equivalent (Vyndamax®) is also available. Side effects are uncommon but may include diarrhea, urinary tract infection, vaginal infection, and stomach pain. (Pfizer, Inc.) www.vyndamax.com

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 amyloid fibrils.

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

Acoramidis was generally well tolerated. The most commonly observed side effects in clinical trials were cardiac failure, AFib, COVID-19, acute kidney injury, shortness of breath and constipation. Acoramidis is taken by mouth at 712 mg twice a day. BridgeBio (Palo Alto, CA, USA) www.bridgebio.com.

Organ transplantation

Depending on damange to the heart, a heart transplant may be considered. Transplantation, though well-established, is costly and high-risk. Post-transplant complications are common. Outcomes depend on age of onset and progression of disease.

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.

DOLOBID® (DIFLUNISAL; OFF-LABEL)

Diflunisal is a medication that has been used for arthritis for many years but has also been found to stabilize TTR and prevent misfolding. In fact, tafamidis was designed to act similarly to diflunisal, but with less side effects. Diflunisal side effects include gastrointestinal upset, gastric ulcers, worsening edema, or kidney injury, however, in select patients it is very well tolerated.

DOXYCYCLINE (OFF-LABEL)

Doxycycline is an antibiotic that may disrupt or degrade amyloid

fibrils. Doxycycline studies in patients with ATTRwt have not yet been conducted, but in small clinical trials in people with advanced cardiac disease, it helped relieve symptoms. Possible side effects include loss of appetite, nausea and vomiting, diarrhea, rash, sensitivity to the sun, and hives.

DOXYCYCLINE/TUDCA (TAUROURSODEOXYCHOLIC ACID; OTC)

TUDCA is a bile salt and liver supplement naturally produced by the gallbladder. Sold OTC and online, it's believed to have many health benefits. Combined with doxycycline, it has shown promise in removing TTR deposits and repairing tissue. A pilot study in patients with ATTR (both wild-type and hereditary) found that 100 mg of doxycycline daily plus 250 mg of TUDCA three times a day halted progression of heart disease and neuropathy for up to a year. It is important to note that more research and studies are needed to confirm these findings.

GREEN TEA (EGCG; OTC)

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.

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.

MANAGING SYMPTOMS

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.

This booklet is designed to give you the latest information on ATTRwt and its treatment. It is not a substitute for medical advice, but it can help protect you from medical errors and inform your interactions with healthcare providers.

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.

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.

GENE SILENCERS

Vutrisiran is an RNA interference (RNAi) gene-silencer designed to inhibit production of the transthyretin (TTR) protein in the liver, thereby reducing the levels of TTR in the body, with the aim of preventing amyloid build-up and organ damage. Vutrisiran has been approved for hATTR patients with polyneuropathy (nerve damage) and is being investigated for both hATTR and ATTRwt patients with cardiomyopathy. Vutrisiran is delivered through a subcutaneous (under the skin) injection administered by a health care professional in a hospital or clinic setting once every three months. www.alnylam.com/alnylam-rnai-pipeline

Eplontersen, formerly known as IONIS-TTR-LRx, is designed to reduce the production of TTR to treat both hereditary and wild-type TTR amyloidosis. The drug uses the liver targeting, ligand-conjugated antisense (LICA) technology, a form of gene silencing therapy. Eplontersen has been approved for hATTR patients with polyneuropathy (nerve damage) and is currently being investigated for both hATTR and ATTRwt patients with cardiomyopathy in the phase 3 clinical trial, CARDIO-TTRansform. (AstraZeneca and Ionis Pharmaceuticals) www.ionispharma.com/ionis-technology/antisense-pipeline

FIBRIL DEGRADERS

Researchers are testing new ways for drugs to deliver their therapeutic benefits; this includes the use of monoclonal antibodies. Monoclonal antibodies have the ability to target a specific protein or harmful cell. Current studies involve the use of monoclonal antibodies to remove pre-existing amyloid deposits within the heart.

Clinical trials are underway to study the effects of **NNC6019-0001**, a monoclonal antibody that targets TTR

deposits. In a phase 1 trial, the tolerability of NNC6019-0001 was proven amongst hATTR and ATTRwt patients with cardiomyopathy. Its safety and effectiveness are being studied further in an ongoing phase 2 trial. (Novo Nordisk A/S) clinicaltrials@novonordisk.com

NI006 is an additional amyloid depleting monoclonal antibody currently in the pipeline. A phase 1 trial has been completed, in which a cohort of patients demonstrated a decrease in cardiac amyloid load after a period of 12 months. A phase 3 trial is expected to begin initiation in early 2024. (AstraZeneca and Nuerimmune) www.astrazeneca-us.com

GENE-EDITING

NTLA-2001 is a CRISPR-Cas9 gene-editing agent designed to treat ATTR amyloidosis by reducing TTR protein levels. A phase 1 trial has been completed, in which patients demonstrated a decrease in TTR levels 28 days after a NTLA-2001 infusion. A phase 3 trial is expected to begin initiation in early 2024. (Intellia Therapeutics) www.intelliatx.com/pipeline

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.

SHOULD I PARTICIPATE IN A CLINICAL TRIAL?

Clinical trials are essential for the development of new treatments for patients at all stages of the disease. Your participation in them can speed the approval process for novel therapies and expedite the development of other drugs in their early phases.

Patients who enroll in clinical trials might be among the first to receive the latest drugs and therapies before they come to market. Their effectiveness may be equivalent to already-approved options, more effective, or less so. Unexpected side effects are a possibility and should be considered when weighing risks and benefits of participation.

HOW CAN I FIND A CLINICAL TRIAL?

ARC's amyloidosis clinical trial finder tool, My Amyloidosis Pathfinder (MAP), can help you find a study that might be right for you (www.myamyloidosispathfinder.org). The U.S. government also offers a site than can help you search clinical trials (www.clinicaltrials.gov).

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

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

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 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.

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.

Cardiac biomarkers. Substances released into the blood when the heart is damaged or stressed. Measurements are used to help diagnose conditions associated with insufficient blood flow to the heart.

Cardiac magnetic resonance imaging (CMR). A noninvasive scan that creates detailed images of how well the heart is pumping and if amyloid is present.

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.

Contraindication. A specific situation in which a drug, procedure, or surgery should not be used because it may be harmful to the patient.

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.

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.

Hereditary transthyretin amyloidosis (hATTR). A progressive, systemic disease caused by a mutation in the transthyretin (TTR) gene.

Immunoglobulin light chain amyloidosis (AL amyloidosis). The most 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%.

Proteins. Large molecules that control the structure and function of the body's tissues and organs.

Radionucleotide bone scintigraphy. A noninvasive nuclear imaging technique that uses a dye to show amyloid in the heart and determines the severity of infiltration.

Right sided heart failure. A condition where the right side of the heart is unable to pump enough blood to the lungs; usually caused by high blood pressure.

Right ventricle of the heart. The heart chamber that pumps blood to the lungs.

Transthyretin. A protein produced by the liver that transports thyroid hormone and vitamin A in the blood.

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» *Pfizer*
» *Protego Biopharma*
» *Prothena Biosciences*

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