Treatments and Therapy Options for Alpha-1 Antitrypsin Deficiency

Trea Wallace and Mady Ormon

About The Liver

The liver is an organ located in the upper right upper quadrant of the body. It has 2 distinct blood sources: it receives oxygenated blood from the hepatic artery and nutrient rich blood from the hepatic portal vein. The liver's main functions are regulating chemical levels in the blood and excreting bile.

Bile helps carry waste products away from the liver. The liver, along with its main functions, has over 500 vital functions that it carries out. One of these functions is resisting infections by making immune factors and removing bacteria from the bloodstream.

Source: johnhopkinsmedicine.org

About Alpha-1 Antitrypsin Deficiency

Alpha-1 is a condition that affects the lungs and/or the liver. It is a progressive disease which means it may worsen over time. Alpha-1 can lead to serious lung/liver diseases. About 100,000 people in the United States (and about 100,000 in Europe as well) live with Alpha 1. Worldwide, 1 in every 1,500-3,500 people are affected by Alpha 1.

Alpha-1 can affect people of every race, which was not discovered until recently. As of right now, there is no cure for Alpha-1, only treatments. People with Alpha-1 have an abnormal AAT protein, which means the body has no way to protect itself from damage by its own immune system.

Alpha-1 is genetically inherited. Therefore, it can be diagnosed through blood tests. However, Alpha-1 can also be diagnosed through X-Rays or CT scans of the lungs, pulmonary functioning tests, liver ultrasounds, and liver biopsies.

There are many signs of Alpha-1 Deficiency. Some of these signs affect the lungs, causing shortness of breath, wheezing, chronic coughing with phlegm, frequent chest colds, emphysema, and frequent respiratory infections. However, there are also signs that affect the skin,
such as, jaundice, bleeding, and abdominal swelling.

The effects of Alpha 1 deficiency are brutal. One of the effects is increased risk for lung diseases. Thisvis because AAT protects the lungs from damage, and without those proteins, the lungs are susceptible to so much more damage. The mutated AAT proteins can also damage the liver while trying to leave and aid the lungs, causing increased risk for liver disease among other liver malfunctions.

Source: alpha1.org

Information on Treatments or Therapy Options for Alpha-1 Antitrypsin Deficiency

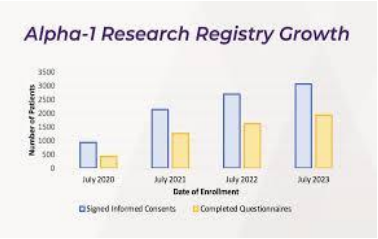
For individuals with alpha-1 antitrypsin deficiency (AATD), there is no approved medication to treat the liver-related health issues, and the only treatment available is liver transplant for very sick livers. There is augmentation therapy available to treat some alphas with pulmonary (lung) disease. Health care providers will discuss different management options with patients such as changes to lifestyle that may help to stop the progression of disease.

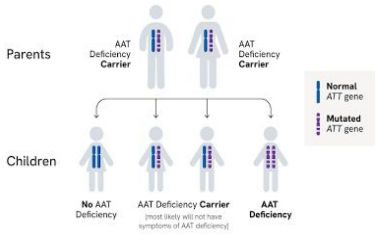
Due to this gap in healthcare, there remains a huge need for research and innovation in AATD. There are different companies and scientists who are at different stages of research to help address this problem. In research, typically there is no "one size fits all" medication, so lots of different types of research and drugs need to be tried in different people.

Depending on where Alpha-1 affects you, treatment options may include:

- **Augmentation therapy.** Your provider can increase your AAT levels by giving you supplemental normal AAT (collected and purified from blood donors) directly into a vein (IV infusion). This doesn't prevent liver damage from Alpha-1.
- **Medication.** Inhalers can make it easier to breathe by reducing inflammation and opening your airways.
- **Oxygen therapy.** If your oxygen levels are low, your provider may prescribe supplemental oxygen, which a machine delivers through a mask on your face or through small tubes in your nose.
- **Pulmonary rehabilitation.** Breathing exercises and physical therapy can make breathing easier.
- **Smoking cessation therapy.** If you smoke, your provider can recommend therapies to help you quit.
- **Lung transplant.** If your lungs are severely damaged, getting a healthy lung through a transplant can help improve your quality of life.
- **Liver transplant.** If your liver is badly scarred, your provider may recommend a liver transplant. A healthy liver should make normal AAT.

Source: Biomarin and my.clevelandclinic.org



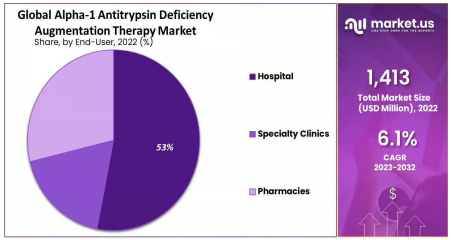


Information on Policies that affect this disease

Since Alpha-1 deficiency is such an overlooked disease, it's important people who struggle with this disease receive proper care. A policy that assures this is the **Affordable Care Act (ACA)** which ensures that individuals with pre-existing conditions, including Alpha-1 deficiency, cannot be denied health insurance or charged higher premiums. In addition the the ACA, there are certain disability rights and benefits that may aid people with AATD. For example, the **Social Security Disability Insurance (SSDI) & Supplemental Security Income (SSI)** may allow individuals with severe AATD related liver or lung diseases to qualify for disability benefits.

Unfortunately, Alpha 1 deficiency being a disease that commonly overlooked means that there are also negative impacts upon people with AATD. For example, many insurance companies have plans with high out of pocket costs, which makes it difficult for AATD patients to afford essential treatment. **Some states have also acquired Medicaid work requirements, which could make it harder for unemployed or disabled people with AATD patients to maintain coverage.**

Source:journal.copdfoundation.org



Information on Treatment Research in Alpha-1

BioMarin's vision is developing first-in-class and best-in-class therapeutics that provide life-changing advances to patients with rare genetic diseases. BMN 349 is beginning to be studied for the treatment of Alpha-1 Antitrypsin Deficiency with a unique mechanism of action that has the potential to transform liver health and with target portable oxygen concentrator (POC).

Takeda's vision is to discover and deliver life-transforming treatments, guided by our commitment to patients, our people and the planet. **Fazirsiran is a potential first-in-class investigational RNA interference (RNAi) therapy designed to reduce the production of mutant alpha-1 antitrypsin protein** (Z-AAT) as a potential treatment for the rare genetic liver disease associated with AATD.

Source: biomarin.com and takeda.com