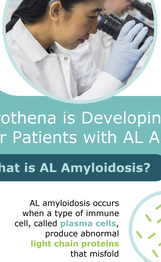
Our Mission is to Make a Real Impact for Patients

prothena



We are pioneering protein dysregulation science to advance novel medicines for diseases caused by misfolded proteins. These devastating conditions include neurodegenerative (e.g., Alzheimer's disease, Parkinson's disease) and **rare systemic amyloid diseases (e.g., light chain [AL] amyloidosis),** which affect millions of people and their families worldwide

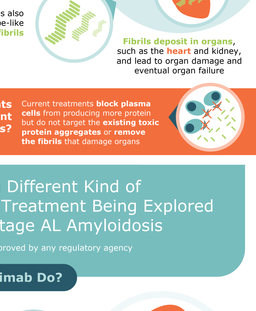
Prothena is Developing a Treatment for Patients with AL Amyloidosis

What is AL Amyloidosis?

AL amyloidosis occurs when a type of immune cell, called **plasma cells**, produce abnormal **light chain proteins** that misfold

These misfolded proteins **clump or aggregate** and can travel through blood vessels, **damaging cells** in different parts of the body

The aggregates also go on to form rope-like structures called **fibrils**



Fibrils deposit in organs, such as the **heart** and kidney, and lead to organ damage and eventual organ failure

Why Do Patients Need New Treatment Options?

Current treatments **block plasma cells** from producing more protein but do not target the **existing toxic protein aggregates** or **remove the fibrils** that damage organs

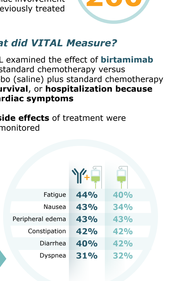
Birtamimab – a Different Kind of Investigational Treatment Being Explored for Advanced Stage AL Amyloidosis

Birtamimab has not been approved by any regulatory agency

What Does Birtamimab Do?

Birtamimab is a **humanized** monoclonal antibody

Birtamimab may block **misfolded light chains** from aggregating, and also **stops the cellular toxicity and organ deposition** of circulating light chain aggregates



Birtamimab also binds to **amyloid deposited in organs**, encouraging immune cells to **remove amyloid** from the body

After the amyloid is removed, the **birtamimab molecule is recycled** to target more amyloid

What Does Humanized Mean?

Humanized means that **birtamimab** has a high similarity to antibodies produced by the human immune system. This reduces the chance that a patient's immune system would recognize **birtamimab** as foreign and react to it

What Has Been Learned About Birtamimab in Clinical Trials?

THE VITAL AMYLOIDOSIS STUDY

Who Were the Patients in the Phase 3 VITAL Clinical Trial?

260 patients with AL amyloidosis and cardiac involvement that were newly diagnosed and not previously treated

What did VITAL Measure?

VITAL examined the effect of **birtamimab** plus standard chemotherapy versus placebo (saline) plus standard chemotherapy on **survival**, or **hospitalization because of cardiac symptoms**

The **side effects** of treatment were also monitored

What Were the Results From VITAL?

VITAL ended early because data analysis suggested that treatment with **birtamimab** would not be able to achieve a significant amount of benefit

Birtamimab was **generally well tolerated**, as a similar percentage of **side effects** was reported by patients treated with **birtamimab** plus chemotherapy and those treated with placebo plus chemotherapy

Fatigue	44%	40%
Nausea	43%	34%
Peripheral edema	43%	43%
Constipation	42%	42%
Diarrhea	40%	42%
Dyspnea	31%	32%

VITAL results were further investigated in a **post hoc analysis**. Post hoc analyses are not planned as part of the main clinical trial and are not considered conclusive in proving a benefit, but can offer additional information about the drug studied. Results were examined in patients with the most advanced cardiac disease – those with **Mayo Stage IV AL amyloidosis**

In this post hoc analysis, **birtamimab** plus standard chemotherapy appeared to result in **59% reduction in the relative risk of death**

In patients with **Mayo Stage IV AL amyloidosis**, the addition of **birtamimab** to chemotherapy **did not result in higher rates of side effects** compared with placebo plus chemotherapy

Results From VITAL Are Being Confirmed in the Ongoing AFFIRM-AL Clinical Trial

After discussions with the FDA, a Phase 3 clinical trial (**AFFIRM-AL**) was designed to **confirm the potential risk reduction** seen in the post hoc analysis of patients with advanced AL amyloidosis in VITAL, in a larger number of patients with **Mayo Stage IV AL amyloidosis**

AFFIRM-AL STUDY

What is the Phase 3 AFFIRM-AL Clinical Trial Measuring?

AFFIRM-AL is looking at the effect of **birtamimab** on **survival, quality of life, and physical functioning** in about **150 patients** from >120 sites in 23 countries

Who Can Be Part of AFFIRM-AL?

Patients may be eligible if they have **Mayo Stage IV AL amyloidosis** and cardiac involvement, are **newly diagnosed** and have **not been previously treated**

What Treatments Are Being Given in AFFIRM-AL?

Approximately 100 patients will receive a **monthly** intravenous infusion of **birtamimab** plus standard chemotherapy, and approximately 50 patients will receive a **monthly** intravenous infusion of placebo (saline) and standard chemotherapy

Find out more about Prothena and the AFFIRM-AL clinical trial

Prothena website

AFFIRM-AL website