Phase I clinical trial of monoclonal antibody 11-1F4 in patients with AL amyloidosis

Technology #cu14269

AL amyloidosis, also called primary or light-chain-associated amyloidosis, is a plasma cell disorder. These cells incorrectly produce an excessive number of light chains, which are a component of normal antibodies. The light chains deposit in various tissues, creating plaques that interfere with organ function. As the most common form of amyloidosis, it is responsible for 1200 to 3200 new diagnoses in the United States each year. The disease typically leads to death within 18 to 36 months of diagnosis. Survival time is further limited to 4 to 9 months with cardiac involvement. Currently, chemotherapy (e.g. melphelan, bortezomib, and/or corticosteroids) and stem cell transplants are used to stop the production of the toxic light chains and extend survival. However, this approach cannot address plaques already formed, and less than 5% of all AL amyloidosis patients survive more than 10 years.

Several therapies for AL amyloidosis are in development. Antibodies from Immunome (N-huMAR) are in pre-clinical development, and NEOD-001 from Onclave/Prothena has completed a phase II study. These antibodies bind light chains already in pathologic amyloid plaques, initiating an immune response that can eliminate the plaques.

This technology is another antibody, 11-1F4, that can bind to amyloid plaques and prompt their removal by the immune system. This mouse antibody is chimerized to make it safer for human use. 11-1F4 binds to a different component of amyloid deposits than other antibodies in development, and has been modified with a radioactive label that allows it to be used for Positron Emission Tomography (PET) scans. PET scans enable visualization of the amyloid plaques in the body, which has the potential to improve diagnosis and prognosis. Finally, 11-1F4 has been shown to bind to plaques in AA amyloidosis, indicating the potential for expanded use in the future. 11-1F4 is currently undergoing Phase I clinical trials to determine the maximum tolerated dose. If it proceeds through clinical trials to the market, it is protected by orphan drug exclusivity and the new biologics exclusivity act.

Labeled antibody to assist with plaque visualization and removal in AL amyloidosis

The 11-1F4 antibody achieves the difficult task of removing amyloid plaques by binding to them and eliciting an immune system response to remove them. This antibody binds to a different component of amyloid deposits than other amyloidosis antibodies in development, which means it has the potential to work more effectively. It
also introduces the possibility for personalized medicine, as an individual patient may have a greater response to one antibody than another based on his or her particular mutations.

Another advantage of the 11-1F4 antibody is its radioactively labeled version that can be used to visualize plaques in a PET scan. Rather than using invasive biopsies that carry risks or indirect tests that may be less accurate, physicians can easily see the extent of the disease. This could allow for more straightforward diagnosis and prognosis of amyloidosis.

11-1F4 has been tested in mice with human amyloid plaques. These experiments confirmed that the antibody bound to the pathologic material and caused an immune reaction to eliminate the plaques. There was no evidence of toxicity in the animals. Now, 11-1F4 is undergoing Phase I clinical trials to determine the safety, tolerance, pharmacokinetics, and possible clinical benefits. The majority of patients have already been recruited for Phase Ia, which is focused on determining the maximum tolerated dose. One dose is given to each patient, with escalating dosages for each participant. There have been no major adverse events so far, and there is evidence of some symptomatic improvement. Phase 1b, in which each patient will receive multiple weekly doses, is expected to begin in late Fall 2015.

**Lead Inventor:**

Suzanne Lentzsch, M.D., Ph.D.

**Applications:**

- Antibody with the potential to eliminate pathologic plaques in AL amyloidosis in Phase I clinical trials
- Allows for the visualization of the plaques via Positron Emission Tomography (PET) scan for diagnosis and prognosis
- Also binds to plaques in AA amyloidosis, so indication could be expanded in the future

**Advantages:**

- Binds to a different component of the amyloid deposits than other AL amyloidosis antibodies, leading to the potential for greater patient response or fewer side effects in some cases
- Only antibody shown to localize to amyloid deposits by PET imaging
- No major adverse events in Phase I clinical trials so far, with evidence of symptomatic improvement
- Protected by both orphan drug exclusivity and the new biologics exclusivity act

**Patent Information:**

Patent Issued (US 8,105,594)

Tech Ventures Reference: IR CU14269

**Clinical Trial Information:**

Phase Ia/Ib Clinical Trial Recruiting (NCT02245867)
Related Publications:


Inventors

Suzanne Lentzsch M.D., Ph.D.