Modifying the IMMUNE RESPONSE IN CELIAC

Leslie Williams, CEO of ImmusanT, discusses the company's research for developing a disease-modifying therapeutic for patients with celiac disease.

Celiac disease is often misunderstood as a lifestyle disease. Unmanaged, celiac can result in chronic anemia, osteoporosis, defective dental enamel issues on the teeth, malnutrition, and other issues related to mal-absorption of nutrients.

A gluten-free diet is the only available treatment for celiac disease, but that is complex and not always effective. Even the most diligent patients can suffer the adverse effects of accidental exposure. The burden on patients is high, because it is impossible to avoid gluten altogether, and minute amounts of gluten can trigger an immune response.

Celiac disease results in chronic inflammatory enteropathy perpetuated by an auto-immune-like reaction to dietary gluten. When a person with celiac disease consumes gluten (proteins in wheat, rye, barley, and oats), the immune system responds inappropriately by activating T-cells specific for gluten epitopes to fight the offending proteins, causing immune activation and acute digestive symptoms such as nausea, vomiting, abdominal pain, and diarrhea.

Leslie Williams

Celiac disease is becoming increasingly prevalent, and it is estimated that the disease currently affects 2 million to 3 million Americans and an estimated 1% of the global population.

ImmusanT is developing a new class of therapeutic vaccines for people with autoimmune diseases such as celiac disease.

The company's epitope-specific immunotherapy platform provides a precision-medicine approach to restoring immune tolerance across a range of diseases.

Epitope-specific immunotherapy is an approach to identify the key fragments of the antigens that drive the immune response in autoimmune diseases, says Leslie Williams, director, founder, president and CEO of ImmusanT.

"In celiac disease, for example, the antigen that drives immune response is gluten, and we have identified the components, the immunogenic fragments of the gluten proteins, that are recognized by T-cells," she explains.

ImmusanT's lead program, Nexvax2, reprograms pro-inflammatory T-cells responsible for celiac disease to stop reacting to gluten.

Nexvax2 is in clinical development with the goal of protecting celiac disease patients against the debilitating effects of inadvertent gluten exposure. ImmusanT's program is the most advanced therapeutic approach for celiac disease in clinical development today that targets the underlying cause.

The company is conducting Phase II trials in the United States, Australia, and New Zealand in patients with celiac disease who carry the immune recognition genes for HLA-DQ2.5.

"Our objective with Nexvax2 is to induce tolerance or non-responsiveness," Ms. Williams says. "In our core trial, we have demonstrated protection in patients against acute symptoms of gluten exposure. The goal is to protect patients acutely and avoid longer term immune-mediated damage to the gut."

The company has conducted five Phase I studies, dosing more than 130 patients. Based on results, ImmusanT has identified a well-tolerated dosing regimen, beginning with a low starting dose and escalating up to a top dose that contains the antigenic load of two loaves of bread.

"By changing the dosing regimen, we have avoided the kinds of symptoms that patients might experience when exposed to ingested gluten," Ms. Williams says. "Our research is highly specific and very targeted toward only those gluten components that are immunogenic."

More broadly, ImmusanT is focused on T-cell mediated diseases in which there is a strong HLA association. "MHC genes that predispose patients to certain autoimmune diseases, and in celiac disease, 90% of patients are positive for HLA-DQ2.5," Ms. Williams explains. "The HLA class II molecule risk association is a key differentiator between an allergy and an autoimmune disease."

Nexvax2 is administered as a subcutaneous injection at a doctor's office for the escalation phase and with maintenance doses administered by the patient with an auto-injector.

"The general feedback we've received from patients is the auto-injector is acceptable in terms of having a treatment that will protect them against the effects of gluten exposure," she says. "On average, celiac patients are inadvertently exposed to gluten three to four times a month, and they can be out of work or out of school for days. A medicine that can protect them against inevitable exposure is important to them."

The company is also conducting research in the area of type 1 diabetes.

Ms. Williams says one thing that differentiates ImmusanT's research approach is that the company doesn't use animal testing as a basis for discovery. ImmusanT uses functional assays using patients' blood.

ImmusanT is a private company that so far has raised $83 million in funding. PV