Multiple Sclerosis NEWS TODAY™
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Microglial activation reduced in 5 of 6 SPMS patients on nasal foralumab

The secondary progressive MS patients were treated in expanded access programs

by *Lindsey Shapiro, PhD* | June 8, 2023

Reductions in microglial activation have been observed in the brains of five of six patients with nonactive secondary progressive multiple sclerosis (SPMS) who received treatment with Tiziana Life Science's foralumab nasal spray.

Microglia, resident immune cells in the brain, are believed to play a role in driving inflammation and nerve damage in conditions such as multiple sclerosis (MS). Their activation can be measured with a PET scan, with reduced activation indicating lower inflammation.

The six patients received treatment in expanded access programs (EAP). Two were treated initially in single-patient access programs, while the other four received foralumab in an intermediate-size expanded access program that will enroll up to eight patients.

All are continuing to receive treatment at the Brigham and Women's Hospital (BWH), in Boston, Massachusetts, and data from the other four patients are expected later this year. The company also is planning to launch a Phase 2a clinical trial of foralumab in nonactive SPMS patients in late 2023.

"There are currently no FDA-approved treatments for [nonactive SPMS]," Tanuja Chitnis, MD, the study's principal investigator, said in a press release, noting that the recent findings are "truly encouraging."

"I look forward to getting the 3-month PET scans results of the next 4 Expanded Access patients later in 2023 and to starting the Phase 2a trial this year," added Chitnis, who also is a professor of neurology at Harvard Medical School and a senior neurologist at BWH.

Foralumab designed to block CD3

Foralumab is an antibody designed to block CD3, a protein on the surface of immune T-cells, which have been implicated in the inflammation that drives MS and other neurodegenerative diseases.

Among the benefits of foralumab observed in preclinical studies, the therapy demonstrated an ability to prevent activation of microglia. These cells stimulate inflammation that contributes to the destruction of myelin, the substance surrounding nerve cells that's progressively lost in MS.

At BWH, foralumab is being tested in people with nonactive SPMS, a type of MS marked by progressive accumulation of disability in the absence of relapses.

All six treated individuals, who continued to experience disability progression while on Ocrevus (ocrelizumab), are receiving foralumab at a 50 microgram (mcg) dose sprayed into each nostril in three-week cycles — three weekly doses for two weeks, followed by a rest week.

Data from the first two patients, who were treated under single-patient access programs, showed the therapy is tolerated well and led to disability improvements (or a reduction in disability), accompanied by a suppression of microglial activity on PET scans.

Early data from those two patients prompted the U.S. Food and Drug Administration to clear an EAP allowing foralumab to be tested in up to eight more patients. The first four were enrolled in that program in November.

Now, Tarun Singhal, MD, director of the PET imaging program in neurologic diseases, and associate neurologist and nuclear medicine physician at BWH, has reviewed the PET scans from these four additional patients after three months of treatment.

“I have determined that 3 out of the 4 patients had a reduction in the microglial PET signal,” said Singhal, who also is an assistant professor of neurology at Harvard Medical School. “When combined with my assessment of the first 2 Expanded Access patients, a total of 5 out of the 6 had a reduction in qualitative microglial PET signal.”

“I look forward to studying more patients … to see if this finding is replicated,” Singhal added.

Awaiting more clinical data

Meanwhile, researchers await clinical data from these four patients in the coming months, which will reveal whether reductions in microglial activation are associated with clinical improvements as they were in the first two trial participants, according to Howard L. Weiner, MD, chairman of Tiziana’s scientific advisory board and co-director of the Ann Romney Center for Neurologic Diseases at BWH.

Weiner noted that to see a drop in microglial activation for all but one patient “is extraordinary,” and made “even more remarkable” given the fact all had failed to respond to Ocrevus.

The upcoming Phase 2a trial will enroll a total of 54 participants with nonactive SPMS who will be assigned randomly to receive a placebo or foralumab at doses of 50 mcg and 100 mcg.

The primary outcome measure will be changes in microglial activation after three months. The company expects to begin screening patients this fall, Weiner said in Tiziana’s webinar announcing the data.

Data from the EAP patients “give us increasing conviction in the potential for a positive outcome,” said Gabriele Cerrone, executive chairman, founder, and acting CEO of Tiziana.

“We believe this trial design will provide a quick validation of our intranasal foralumab asset and will allow the company to proceed to the next clinical phase of development in [nonactive SPMS],” she added.

About the Author

Lindsey Shapiro, PhD Lindsey earned her PhD in neuroscience from Emory University in Atlanta, where she studied novel therapeutic strategies for treatment-resistant forms of epilepsy. She was awarded a fellowship from the American Epilepsy Society in 2019 for this research. Lindsey also previously worked as a postdoctoral researcher, studying the role of inflammation in epilepsy and Alzheimer’s disease.