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Decreased Microglial Activation Observed in Foralumab-Treated Patients With Secondary Progressive MS

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Through an expanded access program, new announced data from a small cohort of patients with non-active secondary progressive multiple sclerosis (na-SPMS) treated with foralumab (Tiziana Life Sciences), an investigational anti-CD3 monoclonal antibody, showed reduction in microglial activation after 3 months on the medication. A phase 2 trial, announced earlier this year, is still on track to begin sometime in quarter 3 of 2023.[1]

According to the brief update, 5 of the 6 individuals included in the program demonstrated a reduction in microglial activation on Positron Emission Tomography scans. In addition to the known links between microglial activation and inflammation, microglia has been involved in the process of destruction of myelin in SPMS, as well as the protective sheath covering of nerve fibers and has contributed to the formation of MS lesions.

"There are currently no FDA-approved treatments for na-SPMS," principal investigator Tanuja Chitnis, MD, professor of neurology, Harvard Medical School, and senior neurologist, Brigham and Women's Hospital, said in a statement.[1] "The reduction in microglial activation in the 3-month PET scans in 5 out of 6 patients is truly encouraging and 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."

Foralumab is designed to bind to T cell receptor and dampens inflammation by modulating T cell function, thereby suppressing effector features in multiple immune

cell subsets. The agent is administered intranasally, providing a novel avenue for treatment of inflammatory human diseases. After feedback from a Type C meeting with the FDA, Tiziana submitted its protocol for the phase 2 study of foralumab in April, with the trial expected to start later this year.

"I believe that Tiziana and Harvard are at the forefront of research in neuroinflammatory diseases with unmet need," Gabriele Cerrone, executive chairman, founder, and acting chief executive officer, Tiziana, said in a statement. "Our Phase 2a multi-center, double-blinded, placebo-controlled trial in na-SPMS uses the 3-month PET scan as the primary outcome measure and our expanded access data from the first 6 patients give us increasing conviction in the potential for a positive outcome. 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 na-SPMS."[1]

In addition to MS, the company is planning to evaluate the agent as a potential treatment for patients with Alzheimer disease. Announced in October 2022, an investigational new drug application (IND) for a phase 1 study is expected to be filed by the third quarter of 2023 upon the completion of requested toxicology studies, with the program beginning by the end of 2023. The decision to file an IND came after Tiziana received an affirmative response from the FDA on a pre-investigational new drug application.[2]

Foralumab has been assessed in patients with mild to moderate COVID-19. Published in August 2021, the study featured 39 outpatients who were randomized to either control (n = 16), intranasal foralumab 100 µg/day given for 10 consecutive days with 6 mg dexamethasone given on days 1-3 (n = 11), and intranasal foralumab 100 µg/day along given for 10 consecutive days (n = 12). All told, investigators observed a reduction of serum interleukin-6 and C-reactive protein in patients treated solely with foralumab vs controls or those on a combination approach. Specifically, foralumab alone resulted in a 69% reduction in IL-6 levels at day 10 (P = .031) and 85% reduction in CRP at day 10 (P = .032).[3]

REFERENCES

1. Tiziana Life Sciences announces reduction in microglial activation in a total of 5 out of 6 intranasal foralumab expanded access patients with non-active secondary progressive multiple sclerosis. News release. Tiziana Life Sciences. June 5, 2023. Accessed June 13, 2023. https://www.biospace.com/article/releases/tiziana-life-sciences-announces-reduction-in-microglial-activation-in-a-total-of-5-out-of-6-intranasal-foralumab-expanded-access-patients-with-non-active-secondary-progressive-multiple-sclerosis/

2. Tiziana Life Sciences plans to submit IND for phase 1 trial of intranasal foralumab in Alzheimer disease patients. News release. Tiziana Life Sciences. October 12, 2022. Accessed June 13, 2023. https://www.tizianalifesciences.com/news-item?s=2022-10-12-tiziana-life-sciences-plans-to-submit-ind-for-phase-1-trial-of-intranasal-foralumab-in-alzheimers-disease-patients

3. Moreia TG, Matos KT, De Paula G, et al. Nasal administration of anti-CD3 monoclonal antibody (foralumab) reduces lung inflammation and blood inflammatory biomarkers in mild to moderate COVID-19 patients: a pilot study. *Front Immunol.* Pubished online August 12, 2021. doi:10.3389/fimmu.2021.709861