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Treatment of six non-active secondary progressive MS patients with nasal anti-CD3 monoclonal antibody (Foralumab): safety, biomarker, and disability outcomes

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Introduction:

There are no effective treatments for non-active secondary progressive MS (SPMS). In EAE, nasal anti-CD3 suppresses disease by inducing Tregs and dampening microglia/astrocyte inflammation (Mayo, 2016), and the antibody does not enter the bloodstream or brain. We found that a fully human anti-CD3 Mab (Foralumab) given nasally to healthy volunteers was safe with immune effects seen at 50ug (Chitnis, 2022). Nasal Foralumab reduced lung inflammation in COVID (Moreira, 2021) and was associated with a regulatory immune signature (Moreira, 2023). We investigated nasal Foralumab in six patients with non-active SPMS, under an FDA expanded access program.

Objectives/Aims:

To determine if nasal Foralumab has a therapeutic effect on patients with non-active SPMS.

Methods:

Six patients (3 females, 3 males) with non-active SPMS and clinical progression despite DMTs were treated. Nasal Foralumab 50ug/day was administered 3x/week for 2 weeks with 1 week rest, constituting a treatment cycle. Clinical assessments were undertaken, MRI and PET brain imaging performed, and serum cytokines and scRNAseq measured.

Results:

Subject EA1 has completed 21 treatment cycles over 1.8 years and EA2 has completed 21 treatment cycles over 1.3 years. There have been no serious treatment-related adverse events, significant nasal irritation, or severe laboratory abnormalities. In EA1, EDSS, pyramidal motor score, T25FW, SDMT, and 9HPT stabilized. Microglial activation measured by [F-18]PBR06 PET scan was reduced 3 months and 6 months after treatment. Serum IFN-γ, IL-18, IL-1ß and IL-6 inflammatory cytokines were reduced and scRNAseq showed immune modulation with upregulation of GIMAP7 and TGFb1 gene expression and downregulation of NKG7 in CD3+ cells. In EA2, after 15 cycles of treatment, EDSS improved from EDSS 6.0 (pre-treatment) to 5.0. EDSS improvement was related to maximum ambulatory distance without cane (> 200 m). Subjects EA3-6 began treatment in December 2022-January 2023 and will complete their 6-month treatment cycle in August 2023. All clinical, laboratory, and available imaging results to date will be presented.

Conclusion:

Nasal Foralumab is a novel, non-toxic immunomodulatory treatment for non-active SPMS. Two patients completed over 12 months of therapy with no severe TRAEs and experienced improved clinical, imaging, and immune biomarkers. 10 patients in total will be treated under the expanded access program and a multi-center placebo controlled double blind trial is planned.

Disclosures:

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