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

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Introduction

Background

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.

Objective and Methods

Objectives/Aims

To determine whether nasal foralumab has a therapeutic effect in patients with non-active SPMS (na-SPMS).

Methods

Six patients (3 females, 3 males) with non-active SPMS (na-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 every 3 weeks, and standardized 3T MRI was performed at baseline, 3 months and 6 months. Additionally, F^{18}-PBR06-microglial PET brain imaging was conducted at 3 months and 6 months, with qualitative analysis performed by TS.

Results

Table 1: Baseline characteristics of the 6 patients with non-active SPMS enrolled in the Expanded Access nasal foralumab program

EA Subject ID	Sex	Race	Age at Foralmab start	EDSS at Foralumab start	Foralumab treatment duration (# 3 week cycles)
EA1	M	White	62	6.0	21
EA2	M	White	42	6.0	24
EA3	F	White	66	6.5	8
EA4	M	White	50	2.5	8
EA5	F	White	64	6.0	8
EA6	F	White	57	6.0	8

Figure 1: EDSS scores and pyramidal scores for EA1-6

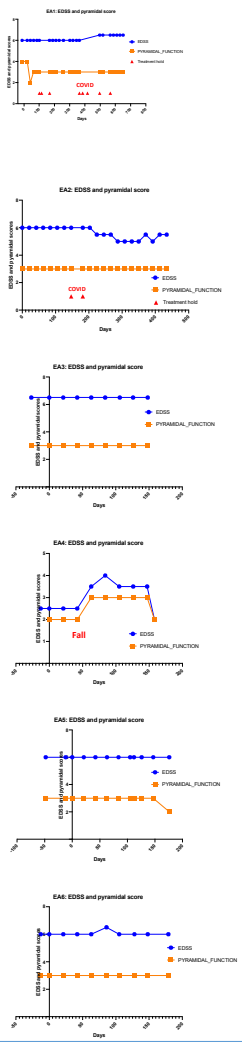

Figure 2: Modified fatigue scale scores (MFIS) for EA1-6

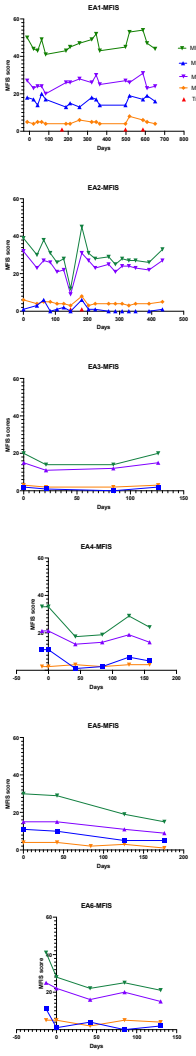

Figure 3: ^{18}F-PBR06-microglial PET brain imaging results: On preliminary evaluation, five out of six EA program patients showed a reduction in PET signal at 3 months, and at 6 months on foralumab treatment, as compared to baseline. EA4 and EA6 images are demonstrated below.

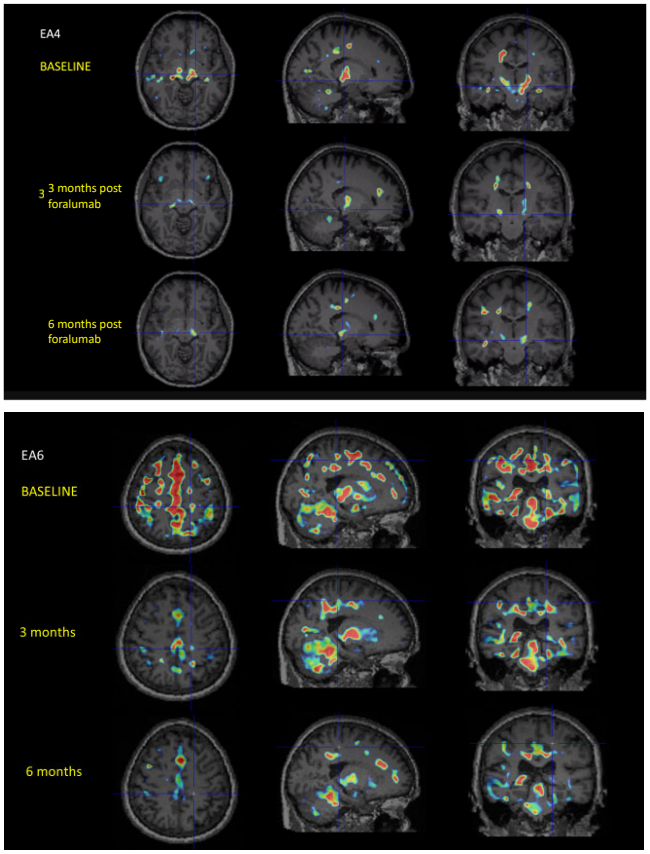

Table 2: Summary of clinical and qualitative PET findings in EA subjects treated with nasal foralumab at 3 and 6 months compared to baseline. No new T2 or Gd+ lesions were noted on post-treatment 3T MRIs.

	EDSS	Pyramidal score	T25FW	MFIS	3 month PET	6 month PET
EA1	–	↓	–	–	↓	↓
EA2	↓	–	↓	↓	↓	↓
EA3	–	–	↓	–	↓	↑
EA4	↓	–	–	↓	↓	↓
EA5	–	↓	↓	↓	↑	↓
EA6	–	–	–	↓	↓	↓

Conclusion

Nasal foralumab is a novel, non-toxic immunomodulatory treatment for non-active SPMS. We report a total of 6 patients on foralumab: 2 patients completed over 12 months of therapy, and an additional 4 patients were treated for 6 months with no severe TRAEs. All 6 patients experienced improvement in at last one clinical measure (EDSS, pyramidal score or MFIS), and 5/6 showed improvement on microglial PET imaging at 6 months. 10 patients in total will be treated under the expanded access program and a multi-center placebo controlled double-blind phase 2 trial is underway.

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