INFORMS-MS
A Phase 2 Placebo Controlled, Double Blind Trial of Intranasal Foralumab

Non-active Secondary Progressive Multiple Sclerosis (na-SPMS)

KOL Call
November 9th 2026



Nasdaq: TLSA

INFORM-MS KOL Call: Forward-Looking Statements and Important Information

Forward-Looking Statements. This presentation may contain forward-looking statements within the meaning of applicable U.S. federal securities laws, including Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These include statements regarding the interpretation and potential implications of INFORM-MS findings, the therapeutic potential of intranasal foralumab, completion and presentation of additional analyses, dose selection, future trial designs, development timelines and planned regulatory discussions.

Forward-looking statements reflect current expectations and assumptions, are not guarantees of future performance and involve risks and uncertainties that could cause actual results to differ materially. These include unsuccessful or inconclusive clinical results; differences between preliminary and final analyses; unexpected safety findings; delays in trial initiation, enrollment or completion; regulatory requirements or decisions; inability to obtain sufficient financing; manufacturing and supply constraints; reliance on third parties; intellectual-property risks; and competition. These risks are not exhaustive, and new risks may emerge. The Company cannot predict all risks or assess the impact of every factor, or combination of factors, on its business. Additional risks are described under “Risk Factors” in the Company’s most recent Annual Report on Form 20-F and subsequent SEC filings. You should not place undue reliance on forward-looking statements.

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INFORM-MS Virtual KOL Call: Meet the Presenters



Tanuja Chitnis, M.D.

Principal Investigator of the INFORM-MS trial

Professor of Neurology, Harvard Medical School / Brigham and Women's Hospital

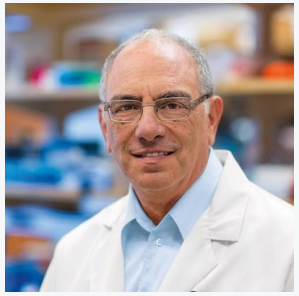


Tarun Singhal, M.B.B.S, M.D., M.B.A.

Founding Director, NeuroPET Program

Ann Romney Center for Neurologic Diseases, Brigham and Women's Hospital, Mass General Brigham

Associate Professor of Neurology, Harvard Medical School



Howard L. Weiner, M.D.

Chairman of Tiziana's Scientific Advisory Board

Robert L. Kroc Professor of Neurology, Harvard Medical School

Co-Director, Ann Romney Center for Neurologic Diseases, BWH



Ivor Elrifi, Ph.D.

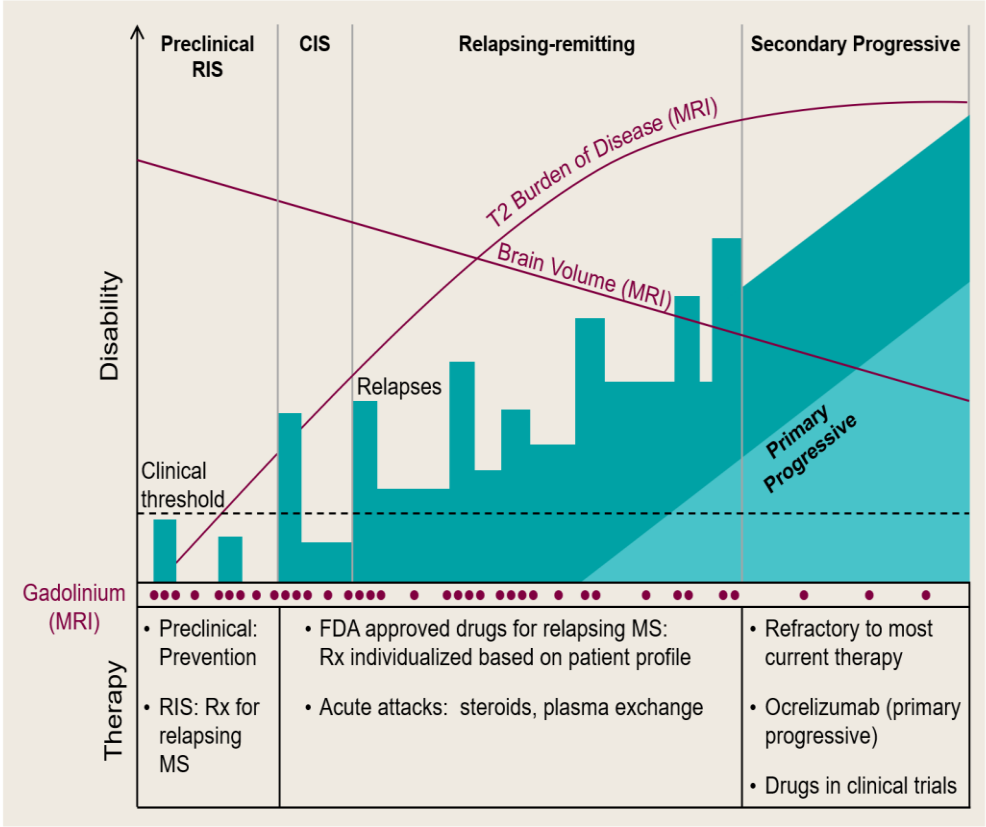
Chief Executive Officer & Executive Director

Tiziana Life Sciences

INFORM-MS: Major Unmet Need in Non-Active SPMS

- No FDA-approved therapies specifically indicated for non-active SPMS
- Patients with progression independent of relapses (PIRA) remain in need of effective therapy
- ~25% of RRMS patients progress to SPMS; substantial portion become non-active
- Fatigue is a major symptom impacting quality of life and daily function
- Current treatments primarily target active/relapsing disease (e.g., ocrelizumab)
- Intranasal foralumab uniquely targets microglial-driven neuroinflammation

Stages of Multiple Sclerosis



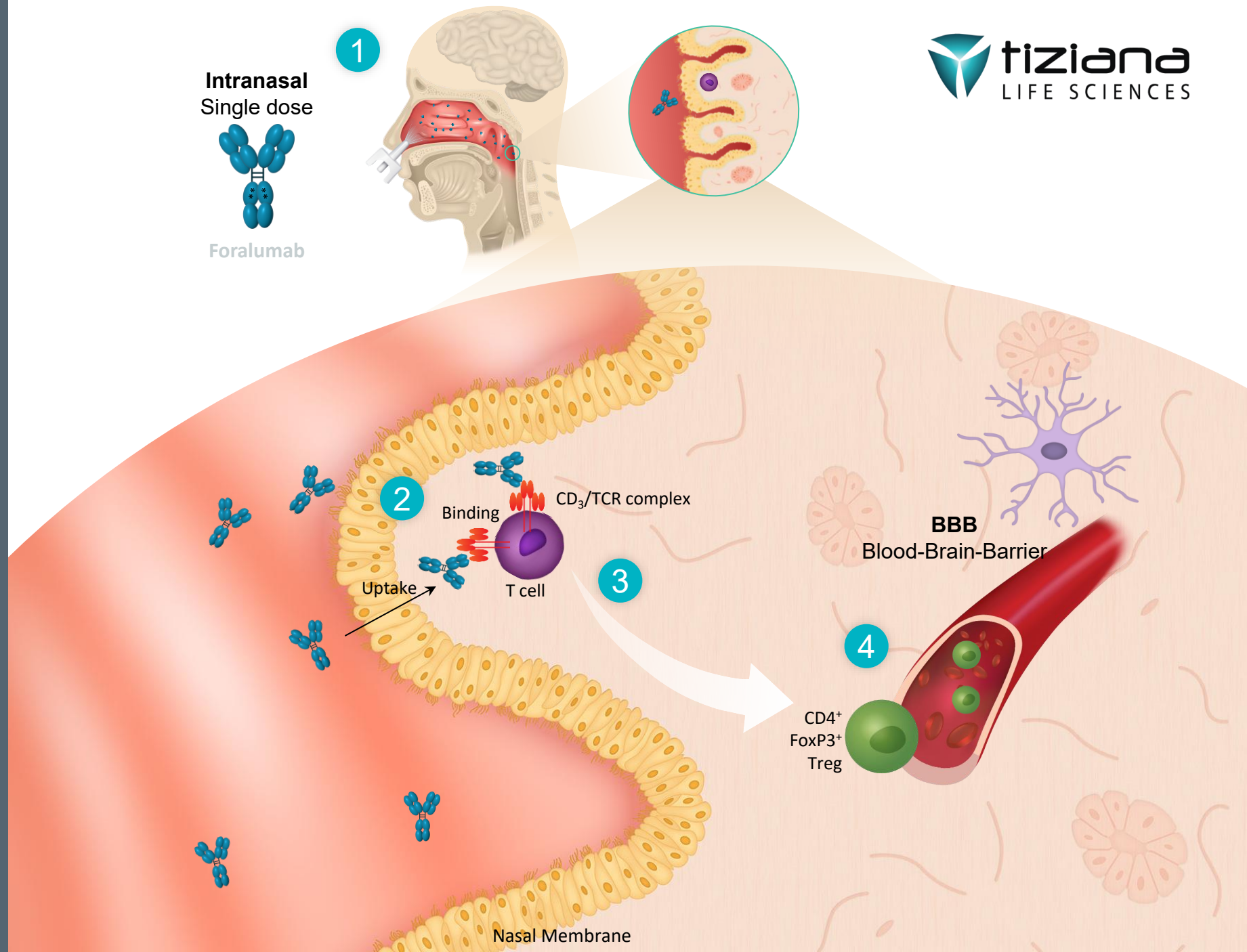
Foralumab: Mechanism of Action[1,2]

Patient inhales the antibody intranasally

Binding of foralumab to the T-cell receptor complex in cervical lymph node

Tregs are then created and activated

These created Tregs then cross the blood brain barrier and regulate the activated innate immune system (microglia).



[1] https://www.pnas.org/doi/10.1073/pnas.2220272120
[2] https://www.pnas.org/doi/10.1073/pnas.2309221120

EXPANDED ACCESS TRIAL

Intranasal Foralumab

Non-active Secondary Progressive Multiple Sclerosis (na-SPMS)



Positive Results With Nasal Foralumab in Expanded Access Program

No Toxicities

No treatment-related toxicities observed
No anti-drug antibodies detected in serum

TSPO PET

8 / 10

Patients Showed Reduced Neuroinflammation After 3 Months Treatment

Fatigue

7 / 10

Patients Improved After 6 Months Treatment

EDSS

10 / 10 Patients Stabilized After 6 Months Treatment

3 / 4 Patients Improved After 12 Months Treatment



RESEARCH ARTICLE OPEN ACCESS

Nasal Foralumab for the Treatment of Progression Independent of Relapses in Patients With Nonactive Secondary Progressive Multiple Sclerosis

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MORE ONLINE
Class of Evidence
Criteria for rating therapeutic and diagnostic studies
NPub.org/coe
Supplementary Material

Abstract

Background and Objectives
Progression independent of relapses (PIRA) is a major therapeutic challenge in multiple sclerosis (MS). Nasal anti-CD3 treats animal models of progressive MS by inducing regulatory T cells (Tregs) that suppress CNS inflammation and lessen clinical disease.

Methods
Ten patients with nonactive secondary progressive MS (naSPMS) that continued to progress on B-cell therapy were treated with nasal anti-CD3 (foralumab) for a minimum of 6 months in an open-label study. Safety monitoring included otolaryngology evaluation and neurologic assessments including Expanded Disability Status Scale (EDSS), MS Functional Composite, Modified Fatigue Impact Scale (MFIS), California Verbal Learning Test, and Low Contrast Visual Acuity. MRI and microglial translocator protein (TSPO)-PET imaging with [F-18] PBR06 were conducted. Serum and CSF proteomic biomarkers and single-cell RNA sequencing of blood were performed to evaluate foralumab-induced immunomodulation. The end points of our study were safety, clinical effects, microglial signal, and immune measures.

Results
Our clinical observations were that all patients stabilized on EDSS scores and 3 of 4 patients treated continuously for 12 months had improvement on EDSS. Six of 10 patients had improvement in fatigue on the MFIS scale. There were no treatment-related serious adverse events or severe AEs, and no new T2 lesions were observed on MRI. There was a reduction in TSPO-PET signal over 6 months ($p < 0.05$). Changes in peripheral blood gene expression occurred as early as 3 months and affected antigen presentation, interferon responses, and regulatory pathways in multiple cell types including FoxP3+ Tregs, $CD4^+$ Tcm cells, $CD8^+$ Tem cells, $CD14^+$ and $CD16^+$ monocytes, and B cells. TGFβ expression was increased across multiple cell subsets.

Discussion
These findings identify a novel, nontoxic immune based therapy for the treatment for PIRA that acts by the induction of a regulatory immune responses and dampens microglial inflammation. Double-blind placebo-controlled trials are warranted to explore nasal foralumab for the treatment of naSPMS.

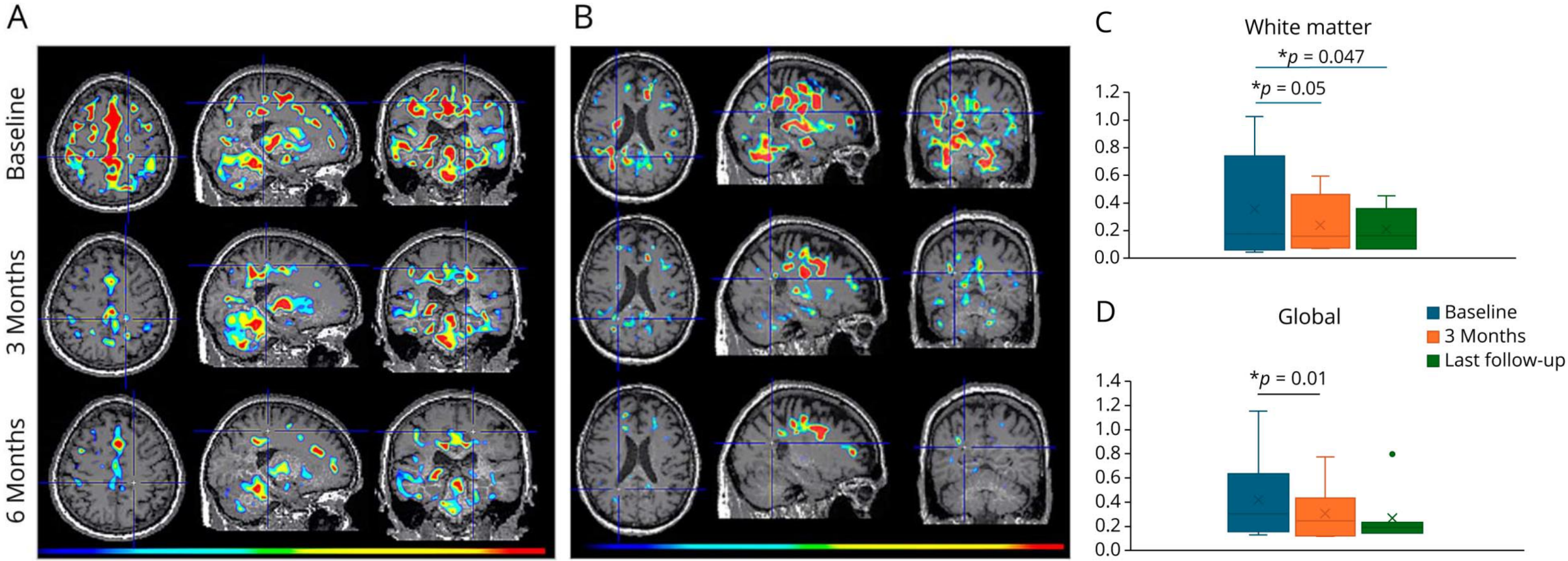
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Nasal Foralumab Reduced Neuroinflammation in Expanded Access Program



Reduced TSPO-PET signal after nasal foralumab treatment. Individualized pGALP z-score maps for patients EA6 (A) and EA1 (B) superimposed on respective patient's T1-weighted MRI demonstrate decreased PET signal after treatment at 3 months (middle row) and 6 months (bottom row) as compared with baseline (top row). Hotter colors represent a higher z-score value and cooler colors represent a lower z-score value as determined by the GALP 2.0 pipeline.
(C and D) White matter and global PET scores at baseline and on treatment. Decreased voxel-wise average [F-18] PBR06-PET mGALP z-scores (GALP 3.0) in white matter (C) and global (D) regions of interest after nasal foralumab treatment for 3 months and 7.5 months (mean duration of treatment at last available PET follow-up visit). GALP = Glial activity load on PET.

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Neurol Neuroimmunol Neuroinflamm 2026;13:e200543. doi:10.1212/NXI.0000000000200543

Nasal Foralumab Modulates Immune Function

Molecular & Cellular Effects in Blood & CSF of na-SPMS Patients Treated with Nasal Foralumab

Results after 6 months nasal foralumab treatment
Increase in regulatory T cells (T_{regs})
Decrease in cytotoxic T cells
Reduced inflammation in spinal fluid

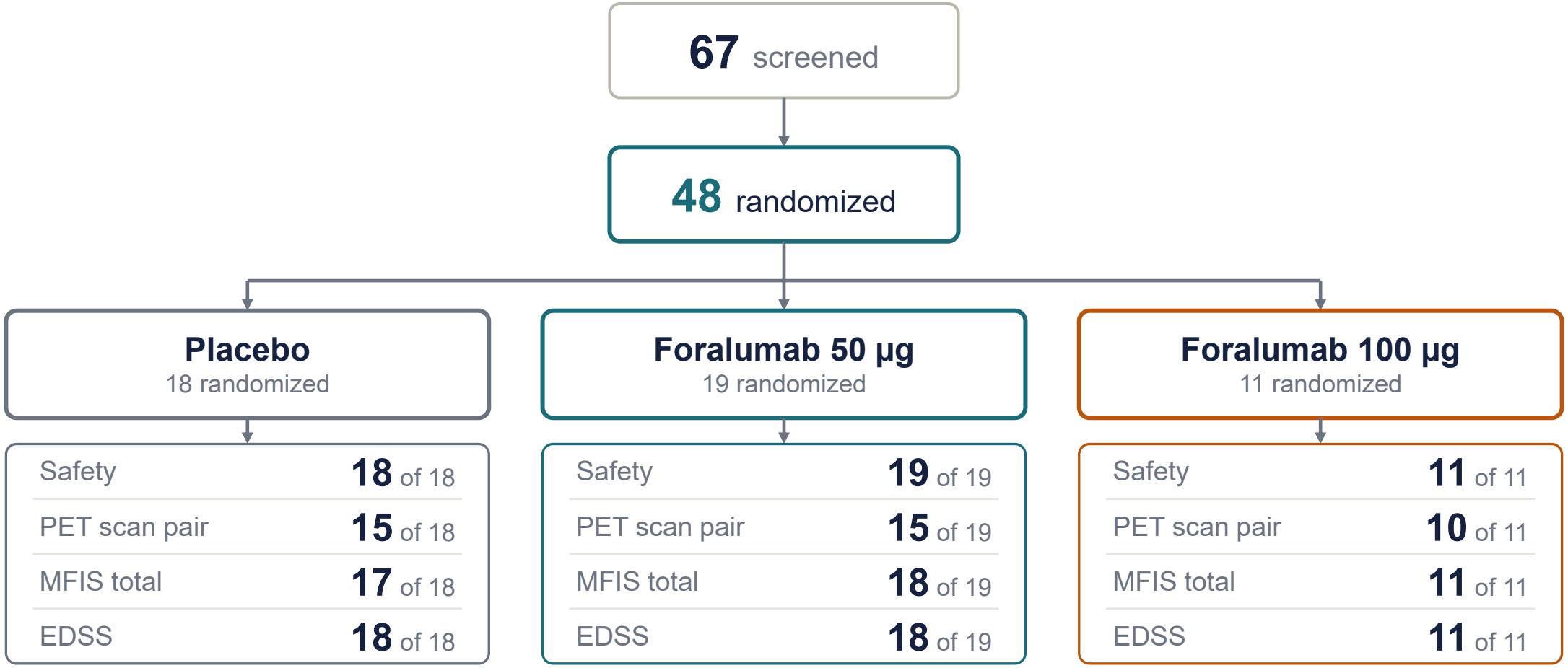
INFORMS-MS TOPLINE DATA

Phase 2 Placebo Controlled, Double Blind Trial of Intranasal Foralumab Confirms Results of EA Program

Non-active Secondary Progressive Multiple Sclerosis (na-SPMS)



INFORM-MS: Participant Flow and Evaluable Data



All participants (48) Safety 48 · PET scan pair 40 · MFIS total 46 · EDSS 47

INFORM-MS: Topline Results Overview

Both primary endpoints (TSPO-PET Neuroinflammation and safety) were met. Secondary MFIS endpoint also met.

PET

Microglial Activation

50 µg vs Placebo

p = 0.0168

Statistically significant reduction in TSPO-PET signal demonstrating decreased microglial activation.

In an exploratory dose arm (100 µg) no significant change in PET signal. Fewer patients enrolled in this arm. Prior data with 250 µg also showed less immunomodulatory effects than the 50 µg dose.

FATIGUE (MFIS)

Clinically Meaningful

Change from baseline → Week 12

–6.17 / –7.18

50 µg (p=0.035) · 100 µg (p=0.040)

Within-arm paired improvements at both doses.

Fatigue is a key driver of quality of life in progressive MS.

SAFETY

Clean Profile

Both doses

No Drug Related SAEs

The first non-invasive anti-CD3 therapy shown to be safe and well tolerated

No study-drug related serious adverse events.

All 48 participants completed treatment

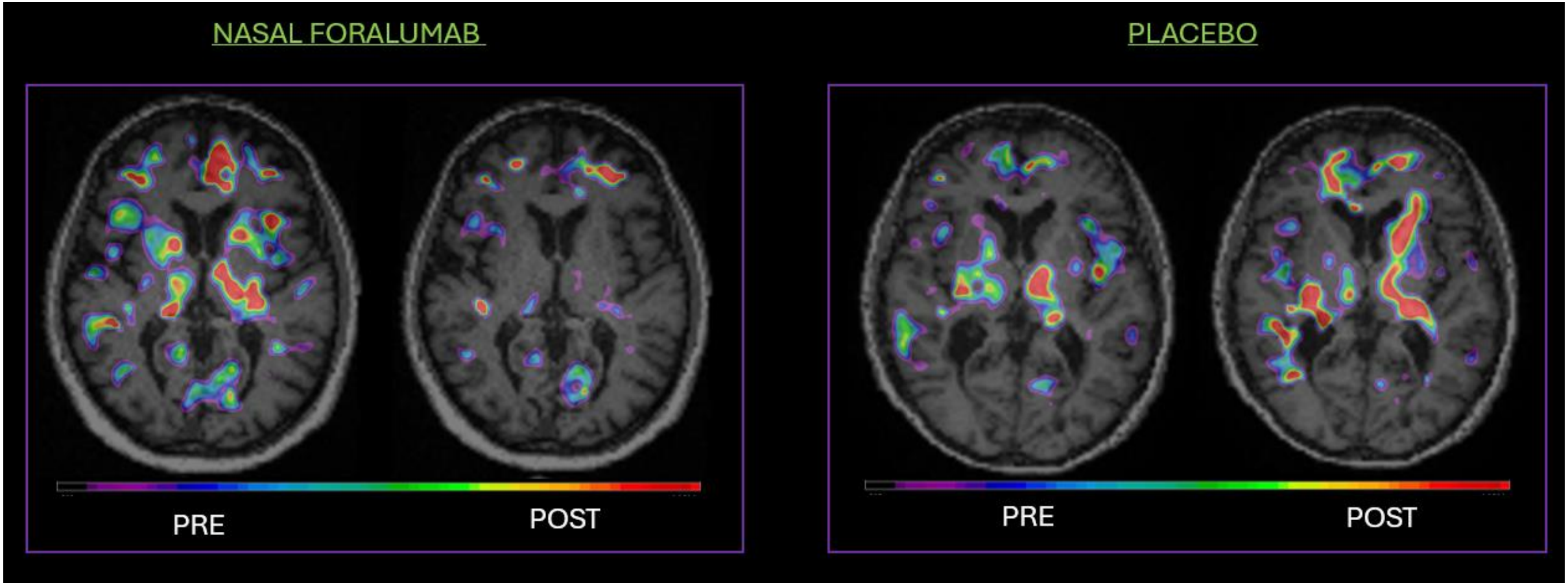
No discontinuations due to AEs.

All 48 participants completed the 12-week treatment period · Both doses safe and well-tolerated · Supports advancement toward registrational path

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INFORM-MS: Neuroinflammation Was Statistically Significantly Reduced

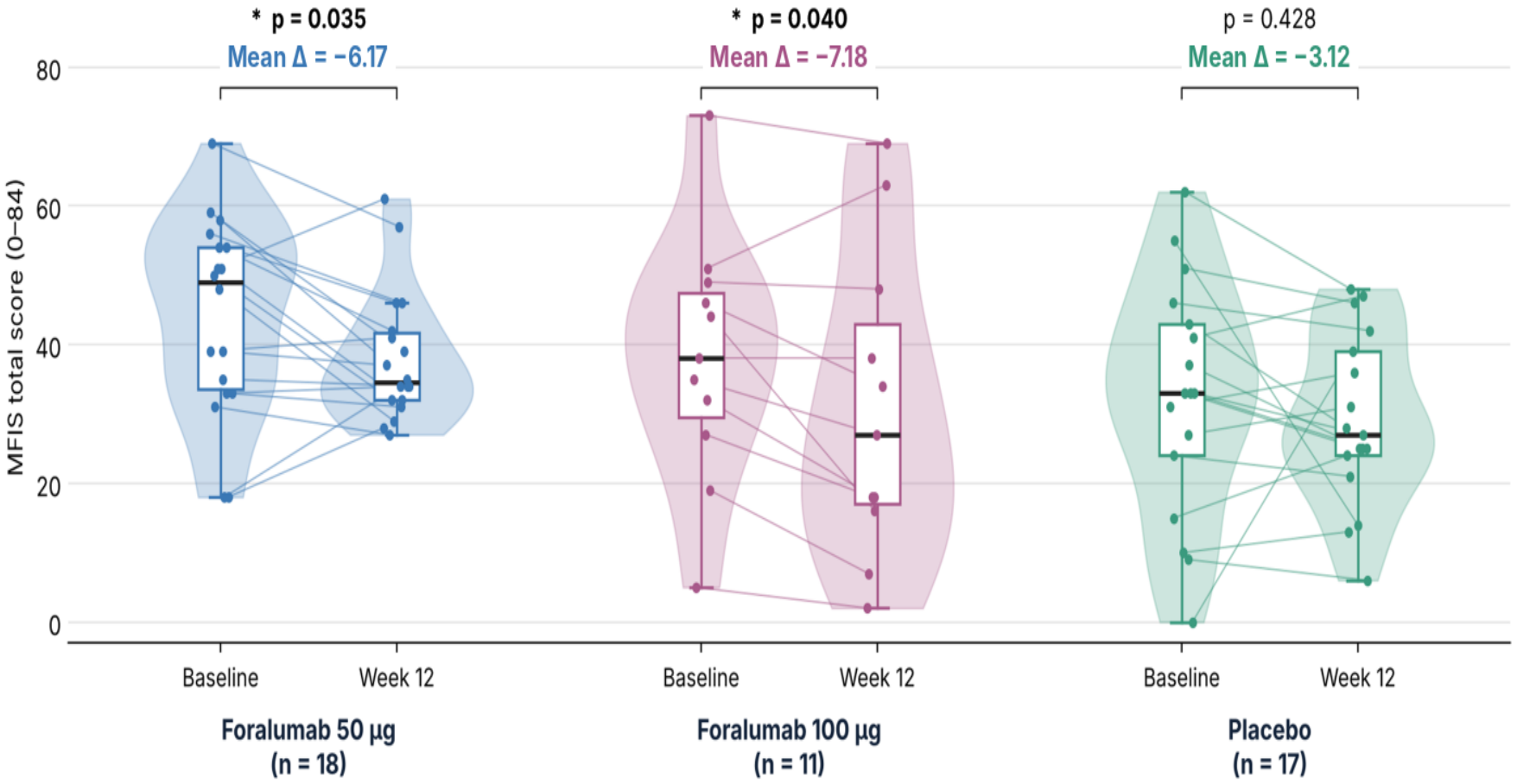
On ANCOVA analysis, [^{18}F]PBR06-TSPO PET demonstrated a significant reduction in globally normalized White Matter SUVR (p=0.0168) after 12 weeks of treatment between the 50 ug nasal foralumab treatment arm and placebo.



Examples of individualized patient mGALP z-score maps following treatment with 50mcg of nasal foralumab and with placebo

INFORM-MS: Nasal Foralumab Reduced Fatigue (Lowered Modified Fatigue Impact Scores; “MFIS”)

MFIS total score, baseline to Week 12





Multiple Sclerosis and Related Disorders 35 (2019) 158–163

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Multiple Sclerosis and Related Disorders

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Clinical trial

Minimally important difference of the fatigue severity scale and modified fatigue impact scale in people with multiple sclerosis

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ARTICLE INFO

Key words:
Multiple Sclerosis
Fatigue
Minimally important difference
Fatigue Severity Scale
Modified Fatigue Impact Scale

ABSTRACT

Background: Fatigue is a common and debilitating symptom of Multiple Sclerosis (MS); however, it is unknown what constitutes a clinically significant change in fatigue. Establishing the minimally important difference (MID) of fatigue outcome measures can inform the interpretation of changes in fatigue by estimating the level of change that is considered clinically relevant.
Aim: Determine the MID for the Fatigue Severity Scale (FSS) and Modified Fatigue Impact Scale (MFIS) in people with MS.
Methods: This cross-sectional study collected information on self-reported fatigue (FSS and MFIS) and quality of life (EQ-5D and MS Impact Scale 29) through an online survey. Anchor-based methods were used to estimate MID, and ordinal logistic regression models were used to determine the difference in fatigue that would predict a significant effect on quality of life.
Results: 365 people with MS (81.9% female, 69.3% relapsing-remitting MS, mean age 46.2 ± 11.6 years, mean time since diagnosis 9.6 ± 8.7 years) responded to the survey. MID estimates for the FSS and MFIS ranged from 0.45–0.88 and 3.86–8.11 respectively, accounting for 6.4–12.6% of maximum FSS score and 4.6–9.7% of maximum MFIS score.
Conclusions: MID estimates derived from this study indicate that a difference of at least 0.45 points on the FSS or 4 points on the MFIS constitutes a clinically significant difference in fatigue. Therefore, these estimates represent a threshold value which can be used to interpret changes in the FSS and MFIS over time or in response to an intervention.

1. Background

Fatigue is a complex symptom of Multiple Sclerosis (MS) that is reported in 70% of the population (Lerdal et al., 2007; Hadjimichael et al., 2008; Rooney et al., 2019), and is often perceived as the most debilitating symptom which significantly impacts upon quality of life (QoL) (Bakshi, 2003). Fatigue may be described as exhaustion, a lack of energy, or overwhelming tiredness which can occur at rest (Mills and Young, 2008), and is commonly defined as “a subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities” (Multiple Sclerosis Council for Clinical Practice Guidelines, 1998). Due to the subjective nature of fatigue, patient reported outcome measures (PROMs) are commonly used to assess the severity and impact of fatigue, and two of the most frequently used in studies involving people with MS are the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (MFIS) (Blikman et al., 2013; Heine et al., 2015; van den Akker et al., 2016).

Interpreting changes in PROMs is important when evaluating the effectiveness of interventions, and it is recognised that conventional statistical analysis provides little information regarding the clinical significance of changes observed following an intervention (Goodman, 1999). However, the interpretation of meaningful changes in fatigue can be enhanced by establishing the minimally important difference (MID) for fatigue PROMs (Revicki et al., 2006). MID, which is defined as “the smallest difference in the outcome of interest which patients perceive as beneficial” (Jaeschke et al., 1989), is a threshold value used to interpret whether a change in an outcome is important from the patient's perspective (Guyatt et al., 2002). MID can be determined using anchor-based or distribution-based methods – the

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MFIS: * p < 0.05 is a within-arm paired t-test; no treatment-versus-placebo comparison is implied (n = 18, 11, 17 with a complete pair).
https://www.msard-journal.com/article/S2211-0348(19)30319-0/fulltext Rooney et al. 2019

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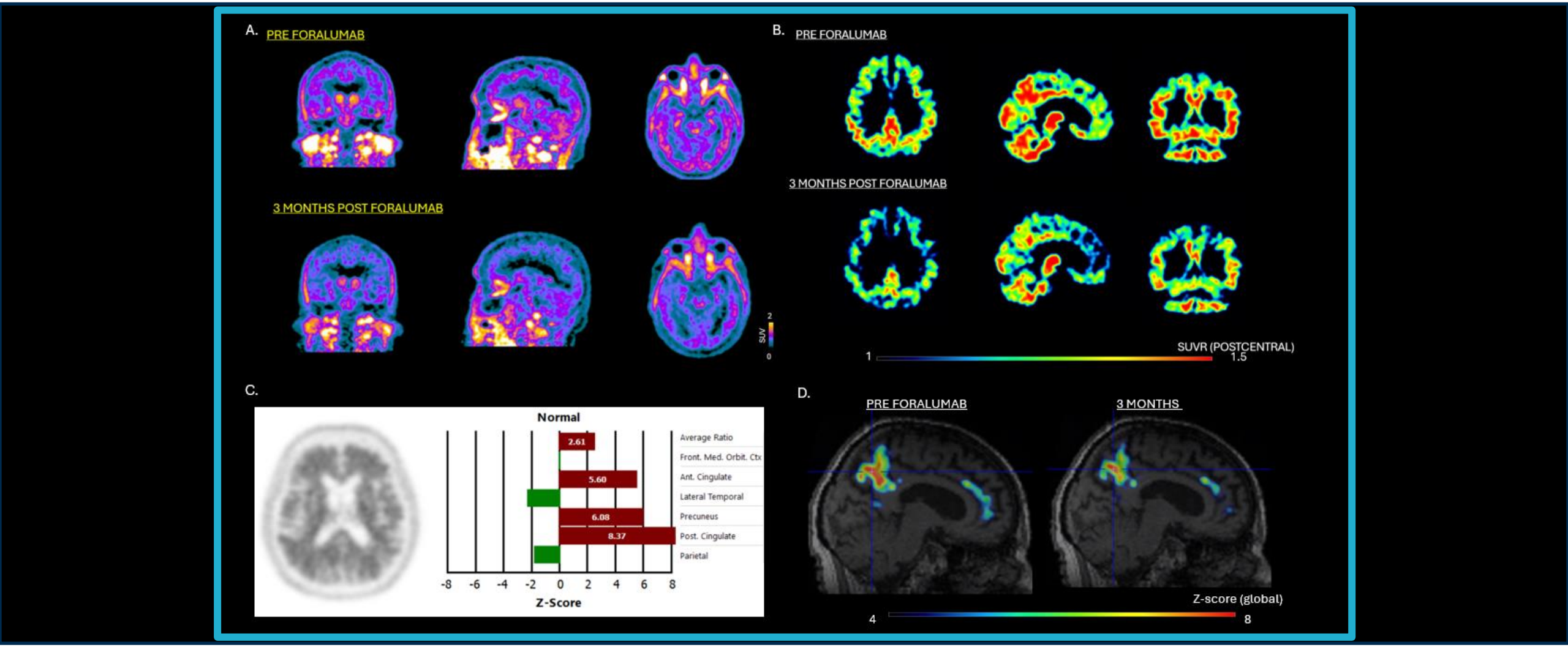
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Intranasal Foralumab Pipeline



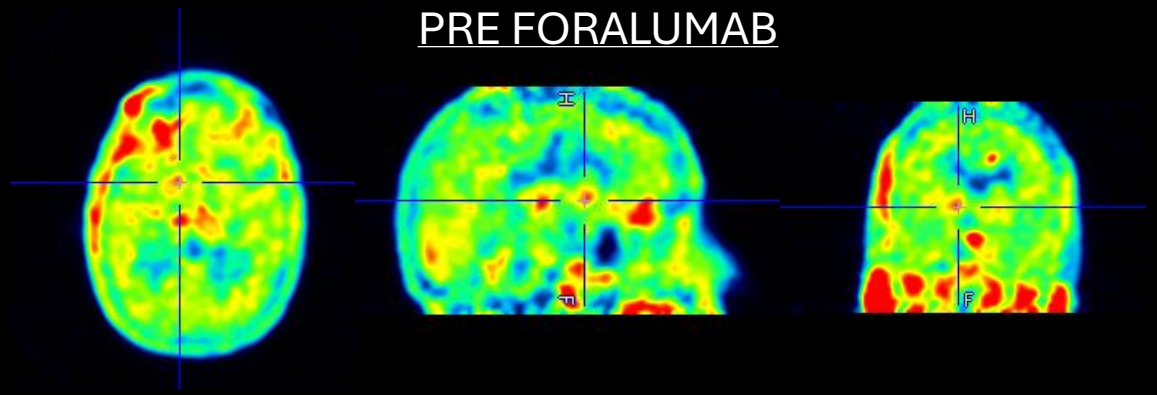
Nasal foralumab dampens microglial activation in Alzheimer's Disease



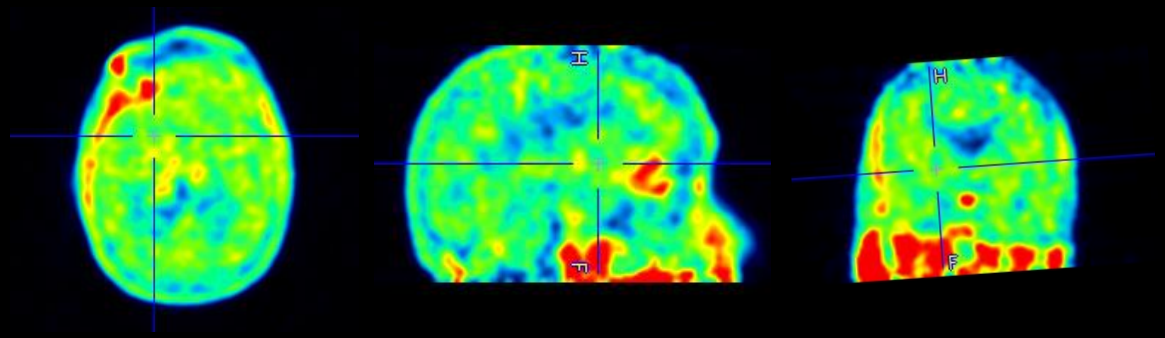
Singhal T, Cicero S, Gale SA, Horan N, Dubey S, Marshall GA, Weiner HL. Dampening of Microglial Activation With Nasal Foralumab Administration in Moderate Alzheimer's Disease Dementia Clin Nucl Med. 2025 Aug 1;50(8):756-757

Nasal foralumab reduces microglial activation in Multiple System Atrophy

PRE FORALUMAB

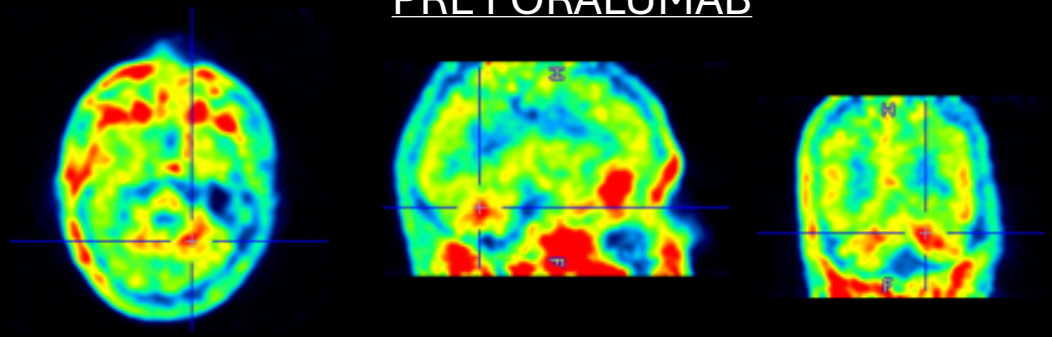


POST FORALUMAB

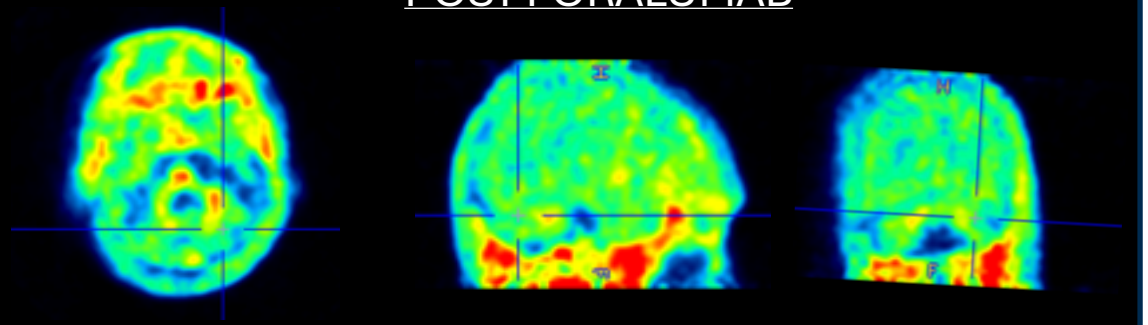


Marked reduction in basal ganglia uptake following nasal foralumab

PRE FORALUMAB



POST FORALUMAB



Marked reduction in Cerebellar white matter uptake following nasal foralumab

Questions



Nasdaq: TLSA

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