# *In Vivo* Nonclinical Evaluation of Activity and Safety of a T Cell Receptor Engineered Regulatory T Cell Therapy for MS Progression Independent of Relapse Activity

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## Abstract

**Introduction:** PIRA is driven by chronic central nervous system (CNS)-localized processes, with a central role for meningeal aggregates, for which no adequate therapies exist. To address this, a cell therapy consisting of Tregs targeted to the CNS by a Myelin Basic Protein (MBP)-specific T cell receptor (TCR) has been developed and underwent nonclinical evaluations. Clinical testing is planned to begin with a Ph1 trial evaluating the safety and dose of this therapy.

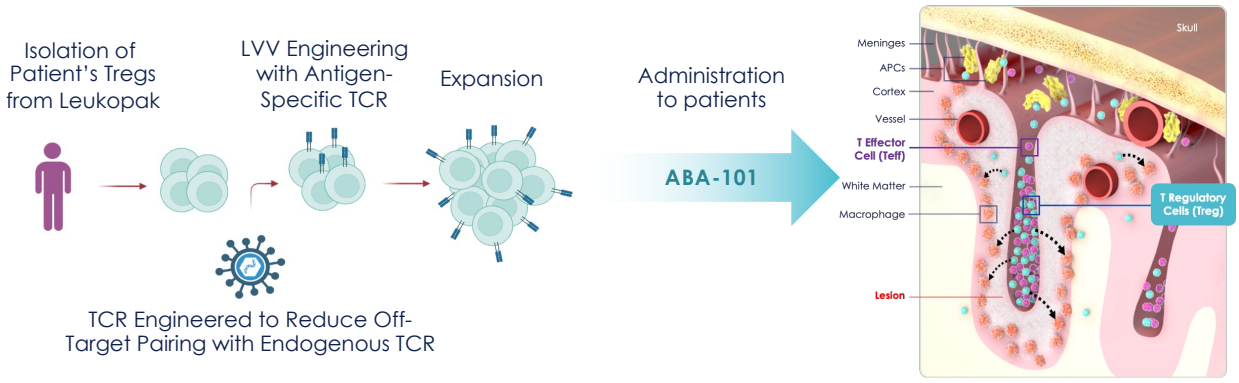
**Objectives/Aims:** To evaluate the safety and therapeutic potential of a regulatory T cell (Treg)-based therapy for the treatment of MS progression independent of relapse activity (PIRA) *in vivo* prior to Ph1 clinical trial initiation.

**Methods:** Animal studies were conducted to evaluate the safety and pharmacology of TCR-engineered Tregs *in vivo using*: 1) an EAE study using a surrogate test article, 2) a xenograft model of inflammation in immune deficient NOD.Cg-*Prkdc*$^{scid}$*IL2rg*$^{tm1Wjl}$/SzJ (NSG) mice and 3) a toxicology study under good laboratory practice (GLP) conditions in NSG mice.

**Results:** In the EAE study, Treg trafficking to the CNS and impact on disease severity were observed. In the xenograft model, TCR-Tregs significantly reduced inflammation-induced weight loss, indicating Treg-mediated suppressive function in an inflammatory setting. In the toxicology study, no therapy-related mortality, organ weight changes, macroscopic or microscopic findings were found. Moreover, TCR-Tregs were phenotypically stable in all studies.

**Conclusion:** *In vivo* studies demonstrate that TCR-engineered Tregs have suppressive capacity and are phenotypically stable in multiple models that can be employed to derisk human TCR-containing T cell therapies. These studies support the safety and therapeutic potential of a TCR-Treg therapy for PIRA and initiation of clinical testing in Progressive MS patients.

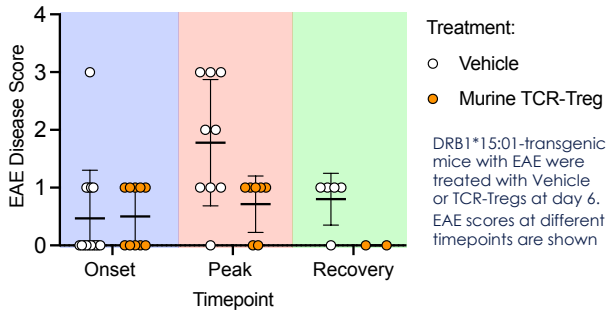
## Autologous TCR-Engineered Treg to Treat Progressive MS




**TCR-Tregs designed to infiltrate CNS targeted inflammation by antigen-specific activation**

## TCR-Tregs Impact EAE Disease Model

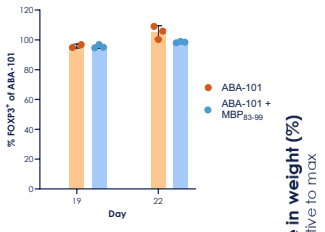
**Murine TCR-Tregs traffic to CNS and persist in EAE model**
**Engineered murine Tregs impact development of disease**




DRB1*15:01-transgenic mice with EAE were treated with Vehicle or TCR-Tregs at day 6. EAE scores at different timepoints are shown

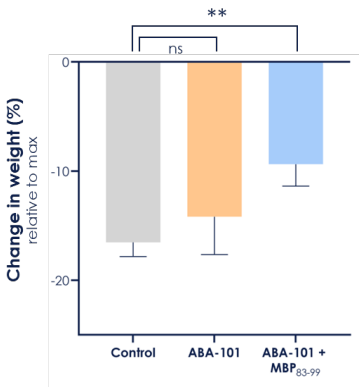
ACTRIMS Forum 2024, February 29 – March 2, 2024, West Palm Beach, Florida. P141 Barrios et al., *Trafficking and Persistence of T Cell Receptor-Engineered Murine Regulatory T Cell (Treg) in a Mouse Model of Experimental Autoimmune Encephalomyelitis (EAE)*. Multiple Sclerosis Journal 2024; 30: (1S) 18–270.

## ABA-101 Mitigates Xenograft Immune Response




**ABA-101 is stable and active in inflammatory conditions**

**ABA-101 retains Treg phenotype and counters xenograft host immune response**




**p=.0121 Mann-Whitney

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