Suggested title:

Immune cell profiles and clinical and safety outcomes with fingolimod in the 12 month FLUENT study of patients with relapsing multiple sclerosis

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Abstract

Background: FLUENT investigated immune cell subset changes in the innate and adaptive immune systems during fingolimod therapy, and their associations with efficacy and safety outcomes.

Objectives: To report changes in immune cell profile, efficacy and safety of fingolimod 0.5 mg/day in adults with relapsing multiple sclerosis (RMS).

Methods: In FLUENT (NCT03257358), a prospective, 12 month, phase 4, multicenter, nonrandomized, open-label study, patients were stratified as fingolimod naive (Cohort 1) or previously treated with fingolimod 0.5 mg/day continuously for ≥2 years (Cohort 2). Primary outcome was change from Baseline to Month 12 in immune cell subsets. Secondary outcomes included Patient Determined Disease Steps (PDDS), anti-John Cunningham virus (anti-JCV) antibody status, serum neurofilament light chain (NFL) concentration, and adverse events (AEs) incidence. Data were analyzed from all patients completing Month 12 follow-up.
Results: 165 patients enrolled in Cohort 1; 217 in Cohort 2. Proportionally more patients in Cohort 1 than Cohort 2 relapsed in the year before baseline. At Baseline, patients in Cohort 1 had proportionally more naive and central memory CD4+ and CD8+ T cells and memory B cells, and proportionally fewer effector memory CD4+ and CD8+ T cells and regulatory B cells, than those in Cohort 2. At Month 12, between-cohort differences in the proportions of these lymphocyte types/subtypes were much reduced or negligible. Levels were essentially unchanged in Cohort 2, indicating reductions in naive T cells and increases in effector memory T cells and regulatory B cells in Cohort 1. Mean baseline PDDS scores were low (Cohort 1, 1.7; Cohort 2, 1.8), and changed little by Month 12. Median change from Baseline in anti-JCV antibody index was small in both cohorts. Proportions of patients with positive JCV serology remained stable at Month 12 (61% and 67% in Cohorts 1 and 2 vs 57% and 65% at Baseline). Mean serum NfL level was higher in Cohort 1 than Cohort 2 at Baseline (12.2 vs 9.6 pg/mL); levels were similar at Month 12 (8.7 vs 9.8 pg/mL), having reduced substantially in Cohort 1. Proportionally more patients in Cohort 1 than in Cohort 2 had treatment-emergent AEs (54.6% vs 44.2%), and discontinued study treatment (12.3% vs 5.5%); 5.5% of patients in each cohort reported serious AEs.

Conclusions: These data expand our knowledge of changes in immune cell profiles over time in patients with RMS treated with fingolimod in the short or long term.

Title character count: 144 / 150 (including spaces)

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**Preferred format:** Oral presentation

**Suggested topic:** Clinical Trials

**Available topics:**

- Biomarkers and Bioinformatics
- Biosensors
- Biostatistical Methods
- Clinical Outcome Measures
- Clinical Trials
- Comorbidities
- Diagnostic Criteria and Differential Diagnosis
- Disease Modifying Therapies – Mechanism of Action
- Disease Modifying Therapies – Risk Management
- Epidemiology
- Experimental Models
- Gender Differences, Hormones and Sex Chromosomes
- Genetics and Epigenetics
- Imaging
- Internet and Social Media
- Machine Learning/Network Science
- Microbiome
- Metabolomics
- Neuromyelitis Optica and Anti-MOG Disease
- Neuro-Ophthalmology
- Neuroprotection, Regeneration and/or Remyelination
- Neuropsychology and Cognition
- Observational Studies
- Pathogenesis – Immunology
- Pathogenesis – Neurodegeneration
- Pathogenesis – Role of Glia
- Pathogenesis – the Blood-Brain Barrier
- Pediatric MS
- Prognostic Factors
- Patient-Reported Outcomes and Quality of Life
- Rehabilitation and Comprehensive Care
- Reproductive Aspects and Pregnancy
- Symptom Management