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# EFFECTIVENESS AND BONE MARROW IMPACT OF OFATUMUMAB IN ITALIAN RRMS PATIENTS

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## INTRODUCTION

Ofatumumab is a fully human monoclonal antibody that is administered by subcutaneous injection once monthly (after initial loading dose) with an autoinjector device. By binding to a unique site on the B-cell marker CD20, **ofatumumab causes depletion of B-cells** via complement-dependent and antibody-dependent cell-mediated cytotoxicity [1].

In pivotal studies, **ofatumumab reduced inflammatory activity**, ARR, by 20,5% in the ASCLEPIOS I and 58,5% in ASCLEPIOS II, p<0.001, and **disability progression** in patients with relapsing multiple sclerosis (RMS) as compared to teriflunomide, maintaining a favorable safety profile [2-4]. Long-term data from the ALITHIOS study showed that continuous **ofatumumab treatment for up to 5 years** led to **sustained efficacy** in relapse rate reduction, profound suppression of lesion activity, and low rates of disability worsening [5].

Compared to anti-CD20 therapies, **ofatumumab may differentially affect newly generated B cells from the bone marrow, potentially preserving long-term immunocompetence and serving as a marker of immunological safety** [6]. **KREC** and **TREC** quantification in peripheral blood allows non-invasive assessment of B- and T-cell output during treatment [6].

# ITAKOS study

**An ITAlian observational, multicenter, 12-month, single-arm study to evaluate the effectiveness and safety of treatment with ofatumumab (Kesimpta®) in a population of 380 RRMS patients in a real-world setting**

## RATIONALE

Filling the knowledge gap on real-world data with ofatumumab in Italian RRMS patients, particularly regarding cognition, fatigue, quality of life and PROs – key indicators of disease burden and treatment impact – while also preliminarily assessing its effect on the peripheral release of newly generated bone marrow–derived B cells.

## POPULATION

- Male or female outpatients ≥18 years old.
- **Patients diagnosed with RRMS**-McDonald criteria 2017 [7].
- Patients **newly treated with ofatumumab**, based on clinical practice and according to the SmPC and to AIFA reimbursement criteria.
- Patient or a legal representative provides written informed consent before any study assessments are performed.

## AIMS

**1° objective: ofatumumab effectiveness-ARR over 12 months.**

**2° objective:** disability progression, cognitive processing speed, fatigue symptoms, QoL, persistence and adherence on therapy, impact on disability during one year of treatment, safety and tolerability, treatment satisfaction, and **NFL** levels.

**Exploratory objectives:** measurement of circulating newly generated B and T lymphocytes using **KRECs** and **TRECs**; effects of ofatumumab treatment on the immunophenotype in peripheral blood through absolute and relative counts of B- and T-lymphocyte subsets; potential neuroinflammatory changes during treatment by measuring **GFAP**.

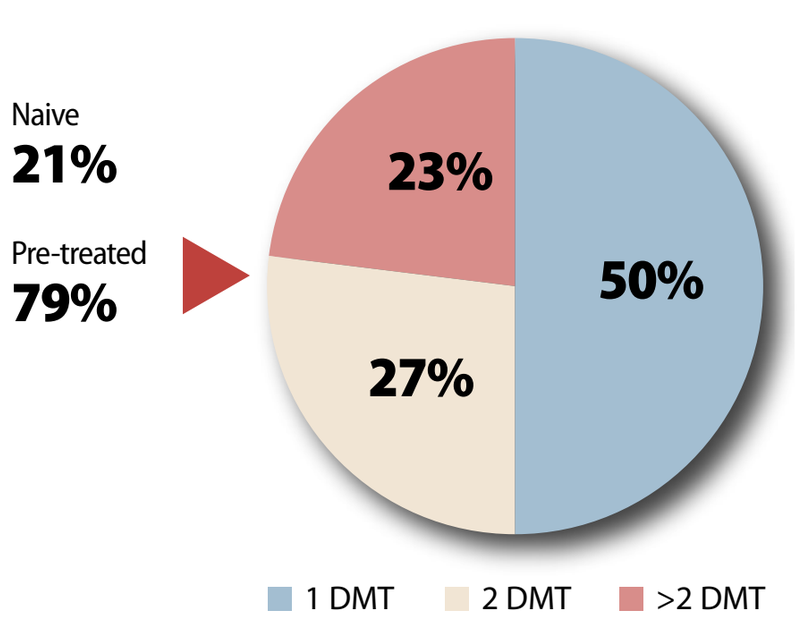
## DATA AND SAMPLE COLLECTION TIMELINE

- Clinical data: during 12 months of treatment.
- Blood sample: at baseline (T0), 6 months (T6), and 12 months (T12) for NFL, GFAP, KREC, TREC, and immunophenotype.

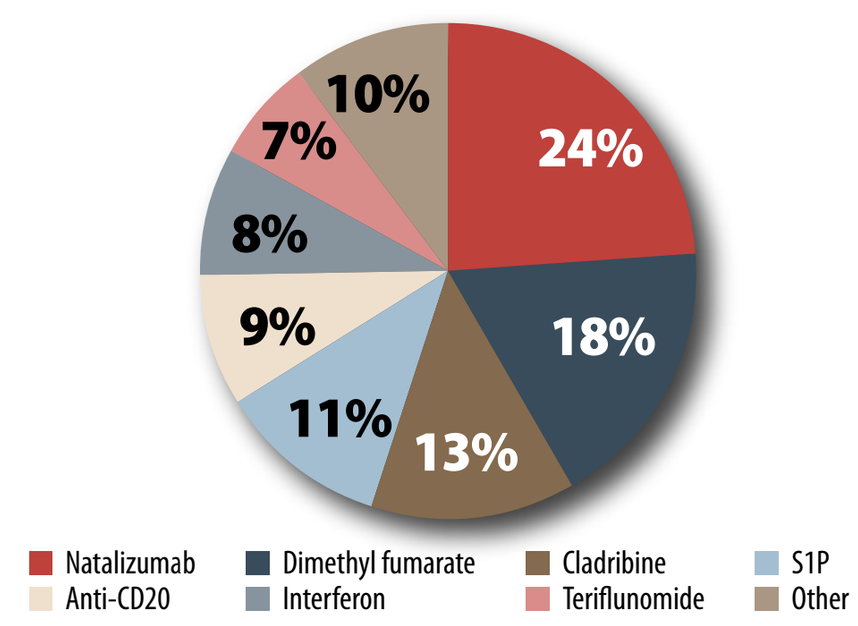
## BASELINE CHARACTERISTICS OF ENROLLED POPULATION

| Population, n | 300 |
|---|---|
| Female, % (n) | 72.7% (218) |
| Age, years, mean (± SD) | 39.6 (±10.7) |
| Disease duration, years, mean (±SD) | 8.2 (±7.08) |
| EDSS, mean (±SD) | 2.2 (±1.5) |
| SDMT, mean (± SD) | 50.9 (±12.6) |

**Treated population**




**Treatments before ofatumumab**




The patients enrollment began in **June 2024**, with the first patient enrolled on July 30, 2024; up to **May 2025**, **300 patients** were involved.

At baseline, **21%** of patients were ofatumumab-**naive**. The remaining 79% of patients had prior DMT exposure. Among them, 50% had received one DMT, 27% had received two, and 23% had received more than two.

Natalizumab, dimethyl fumarate, and cladribine were the **most common treatments** before initiating ofatumumab.

As per protocol, an **interim analysis** is planned once the **100th patient** has completed the **one-year** observation period.

**References 1.** Bar-Or, A., et al., 2022. DMT11. Presented at the Annual meeting of the Consortium of Multiple Sclerosis Centers. **2.** Samjoo, I.A., et al., 2020. J. Comp. Eff. Res. 9, 1255–1274. **3.** Wiendl, H., et al., 2023. Presented at the European Academy of Neurology (EAN). **4.** Hauser, S.L., et al., 2020. N Engl J Med 2020; 383, 546–557. **5.** Kappos, L., et al., 2023. Presented at the European Academy of Neurology (EAN). **6.** Chiarini, M., et al. 2013. J Pub Health Res 2, jphr.2013.e3 **7.** Thompson AJ, et al. 2018. Lancet Neurol.17:162-173. **Abbreviations** ARR, annualized relapse rate; EDSS, Expanded Disability Status Scale; GFAP, glial fibrillary acidic protein; KREC, kappa-deleting recombination excision circles; NFL, neurofilament levels; PRO, patient reported outcomes; RRMS, Relapsed/Remitted Multiple Sclerosis; SDMT, Symbol Digit Modality Test; SmPC, summary of product characteristics; TREC, T-cell receptor excision circles