Ofatumumab in Relapsing Multiple Sclerosis: Real-World Safety data and Implications for Early Intensive Treatment

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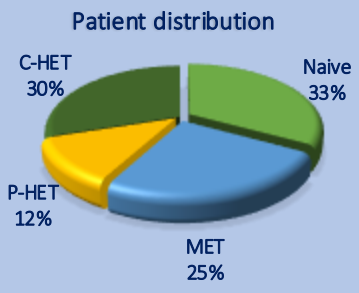
Introduction: Ofatumumab (OFA) is a subcutaneous, fully human anti-CD20 monoclonal antibody approved for the treatment of Relapsing Multiple Sclerosis (RMS). Although OFA efficacy has been substantiated by pivotal trials and observational studies, real-world data on its safety profile are still lacking.

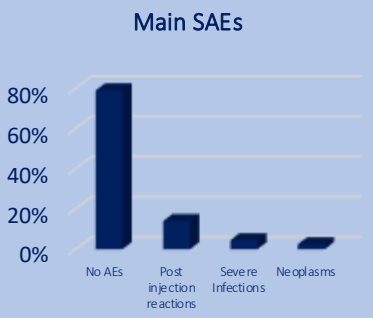
Objective: To evaluate serious adverse events (SAEs) in a OFA real-world RMS cohort.

Materials: This is a longitudinal retrospective study of 249 RMS patients treated with OFA at MS Center of Bari, Italy, between 13 March 2022 and 23 March 2025.

Methods: MS patients OFA treated were stratified in naïve vs. previously treated; disease-modifying therapies (DMTs) were classified as moderate-efficacy (MET: Interferons, Glatiramer acetate, Teriflunomide, Dimethyl fumarate, Azathioprine), continuous high-efficacy (C-HET: Fingolimod, Ozanimod, Siponimod, Ocrelizumab, Natalizumab), or pulsed high-efficacy (P-HET: Cladribine). Safety data were assessed by reporting injection-related reactions, infections, and malignancies every three-six months during the patient follow-up. Key predictors of safety events were assessed by multivariate regression analysis ($p < 0.05$).



Results: The mean follow-up was 1.46 years (± 0.86). EDSS was 2.91 (± 1.32); the disease duration was 8.73 (± 8.44) years. Among the cohort 33% were treatment-naive. Post-injection reactions occurred in 14% of patients. Infections were reported in 4.5% of patients, with none occurring in treatment naive group. Patients previously treated with C-HET had a significantly higher risk of developing infections compared to naive patients ($p < 0.05$, OR 4.35). Furthermore, each additional prior treatment, increased the risk of infection by 62% ($p = 0.04$, OR 1.62). Neoplasms were observed in one patient with a case of mycosis fungoides which led to treatment discontinuation. OFA was stopped in one patient due to myocardial infarction and in two patients following first positive pregnancy tests. One pregnancy is ongoing, while the other resulted in a full-term natural delivery of a healthy infant.



Discussion: Real-world data from this cohort confirm a low occurrence of SAEs, supporting the overall favorable safety profile of OFA. Patients starting OFA as an early intensive treatment (EIT) experienced a reassuring safety profile. The increased risk of infections observed in patients previously treated with C-HET may reflect immunosenescence, potentially leading to a diminished immune response to infectious agents.

Conclusions: Our findings support the safety of an EIT strategy with OFA, without increased risk of SAEs compared to an escalation approach. Emerging pregnancy data may prompt a re-evaluation of current recommendations regarding preconception discontinuation.

References
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