EFFICACY AND SAFETY OF OCRELIZUMAB IN A REAL-WORLD SETTING: A MONOCENTRIC OBSERVATIONAL STUDY

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INTRODUCTION

Ocrelizumab (OCR) is a highly effective therapy approved for the treatment of Relapsing-Remitting (RRMS) and Primary-Progressive (PPMS) Multiple Sclerosis.

Although 10-year data from randomized controlled trials support a favorable risk-benefit profile, real-world data remain limited.

AIMS

To evaluate the long-term **EFFICACY** and **SAFETY** of OCR in a real life cohort of persons with MS (PwMS)

METHODS

We analyzed demographic and clinical data extracted from the clinical chart of pwMS followed at the MS Center of Tor Vergata University Hospital, Rome, who received at least one standard dose of ocrelizumab (600 mg) and had at least 6 months of clinical follow-up (FUP) and with no previous exposure to antiCD20 or having a pregnancy during FUP.

Demographic, clinical (MS characteristics, clinical relapse, EDSS, Progression Independent of Relapse Activity *[PIRA]*, Clinical Disability Worsening *[CDW]*, Clinical Disability Improvement *[CDI]*) and radiological (new or enlarged T2 and Gd+ lesions) data at different time points (Figure 1) were collected. Predictors of disease reactivation (clinical relapses and MRI activity) and progression (*EDSS scores, PIRA, and CDW*) were explored, together with CDI. Information on adverse events such as lymphocytopenia, hypogammaglobulinemia, infections, malignancies, and other relevant medical conditions was also recorded.

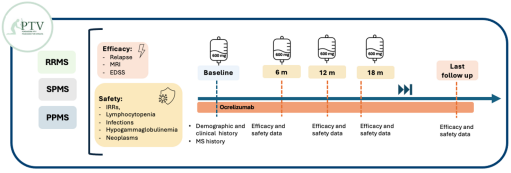

Fig 1: Study design

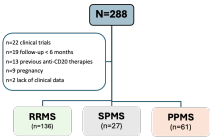

Fig 2: Study cohort

RESULTS

223 patients were enrolled in the study; baseline demographic and MS characteristics at OCR start are summarized in Table 1.

EFFICACY

Over the follow-up period, 22 (**9.9%**) PwMS experienced **≥1 relapse**, 37 (**16.6%**) had **radiological activity** (new or enlarged T2 lesions, Gd+ lesions). No significant predictor of relapses and radiological activity was found.

PIRA occurred in 52 (**23.3%**) pwMS and **CDW** in 76 (**34%**). Among all predictors evaluated (demographics and MS history, Body Mass Index, Body Surface Area, relapses), **baseline EDSS** emerged as the only significant **predictor of PIRA and CDW** (respectively [HR = 1.28, p=0.03] and [HR= 1.39, p=0.00]).

CDI occurred in 39 (17.5%) pwMS. In the multivariate analysis, **longer disease duration** [HR=0.931, p = 0.005] and **higher BMI** [HR= 0.916, p = 0.038] were independently associated with a **reduced probability of CDI**, whereas higher baseline EDSS showed only a trend toward increased risk [HR= 1.171, p = 0.057].

	Full cohort (n=223)	RRMS (n=135)	PPMS (n=61)	SPMS (n=27)
Female sex, n (%)	113 (50,9%)	87 (64,4%)	17 (33,3%)	9 (33,3%)
Age at Ocre start (years), mean ± SD	39,81 (±9,65)	36,28 (±8,97)	45,11 (±8,36)	45,52 (±7,49)
Smoke, n (%)	63 (28,2%)	58 (42,9%)	34 (55,7%)	7 (25,9%)
BMI, mean ± SD	24,4 (± 4,62)	24,1 (±5,09	24,8 (±3,88)	24,8(±3,55)
Autoimmune comorbidities	48 (21,5%)	32 (23,7%)	9 (14,7%)	7 (25,9%)
MS duration (years), mean ± SD	9,8 (±7,97)	8,3 (±7,26)	10,8 (±7,46)	15,7 (±9,06)
ARR 12 months pre Ocre	0,65	0,86	0,34	0,33
Baseline EDSS, median (range)	3 (0-8)	2 (0-7,5)	5.5 (2-7,5)	4,5 (2-8)
Follow up (months), median (range)	44 (6-97)	38 (6-97)	60 (6-81)	27 (6-95)

Tab1: Demographic and MS characteristics at OCR start

SAFETY

84 (21.5%) pwMS developed lymphocytopenia (Tab 2).

Lymphocytopenia was associated with older age at OCR initiation (HR=1.05, p=0.006) and **history of lymphocytopenia with prior therapies** (HR=2.80, p=0.001), whereas **naïve pwMS had a reduced risk** (HR=0.29, p=0.015).

74/136 (**54.4%**) pwMS developed **hypogammaglobulinemia during follow-up, mainly IgM (51.4%).**

One or more infectious events were reported in 150/223 (**67.5%**) patients, yielding an **infection event rate of 3.6 for 100 patient/years**. Only 9 (4.0%) patients required hospitalization.

During follow-up, we also recorded **4 cases of skin cancers.**

Patients with LYMPHOCYTOPENIA	n (%)
NO	175 (78,4%)
YES	48 (21.5%)
Grade 1	24 (50%)
Grade 2	23 (47,9%)
Grade 3	1 (2%)
Grade 4	0 (0%)
TOT	223 (100%)

Tab.2: Patients with lymphocytopenia.
Grade 0 (normal): >1000 /mm3, Grade 1: 800-999 /mm3, Grade 2: 500-799 /mm3, Grade 3: 200-499 /mm3, Grade 4: < 200 /mm3

CONCLUSIONS

This study confirmed the favourable risk-to-benefit profile of OCR in a real-world MS cohort. **PwMS with greater baseline disability showed lower therapeutic response**, reliably reflecting reduced efficacy on ongoing neurodegenerative processes.

Increased incidence of lymphocytopenia in older PwMS suggests immunosenescence as a possible underlying mechanism.

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