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EFFECTIVENESS AND SAFETY PROFILE OF SWITCHING FROM NATALIZUMAB TO OFATUMUMAB IN RELAPSING-MS: A MULTICENTRE REAL-WORLD STUDY

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INTRODUCTION

Natalizumab (NTZ) and Ofatumumab (OFA) are effective RRMS treatments, however, NTZ is linked to progressive multifocal leukoencephalopathy (PML). In this prospective real-world study, we evaluated OFA as an NTZ exit strategy

AIM

To assess the safety, efficacy, and patient satisfaction of Ofatumumab (OFA) as a replacement for Natalizumab (NTZ) in relapsing multiple sclerosis (RMS) patients at high risk of PML or with active disease.

METHOD

42 RRMS patients (mean age 38.1±10.1 years; 69.1% female) from nine Italian MS centers switched from NTZ to OFA due to disease activity evidence (EDA) or high PML risk (for safety). Monitoring lasted >3 months. We collected data on annualized relapse rate (ARR), progression independent of relapse activity (PIRA), PML/severe infections, Treatment Satisfaction Questionnaire for Medications (TSQM) scores and Multiple Sclerosis Impact Scales (MSIS-29) at baseline and after 3, 6, and 12 months. MRI activity was assessed at 3 and 12-months MRI scans from baseline.

RESULTS

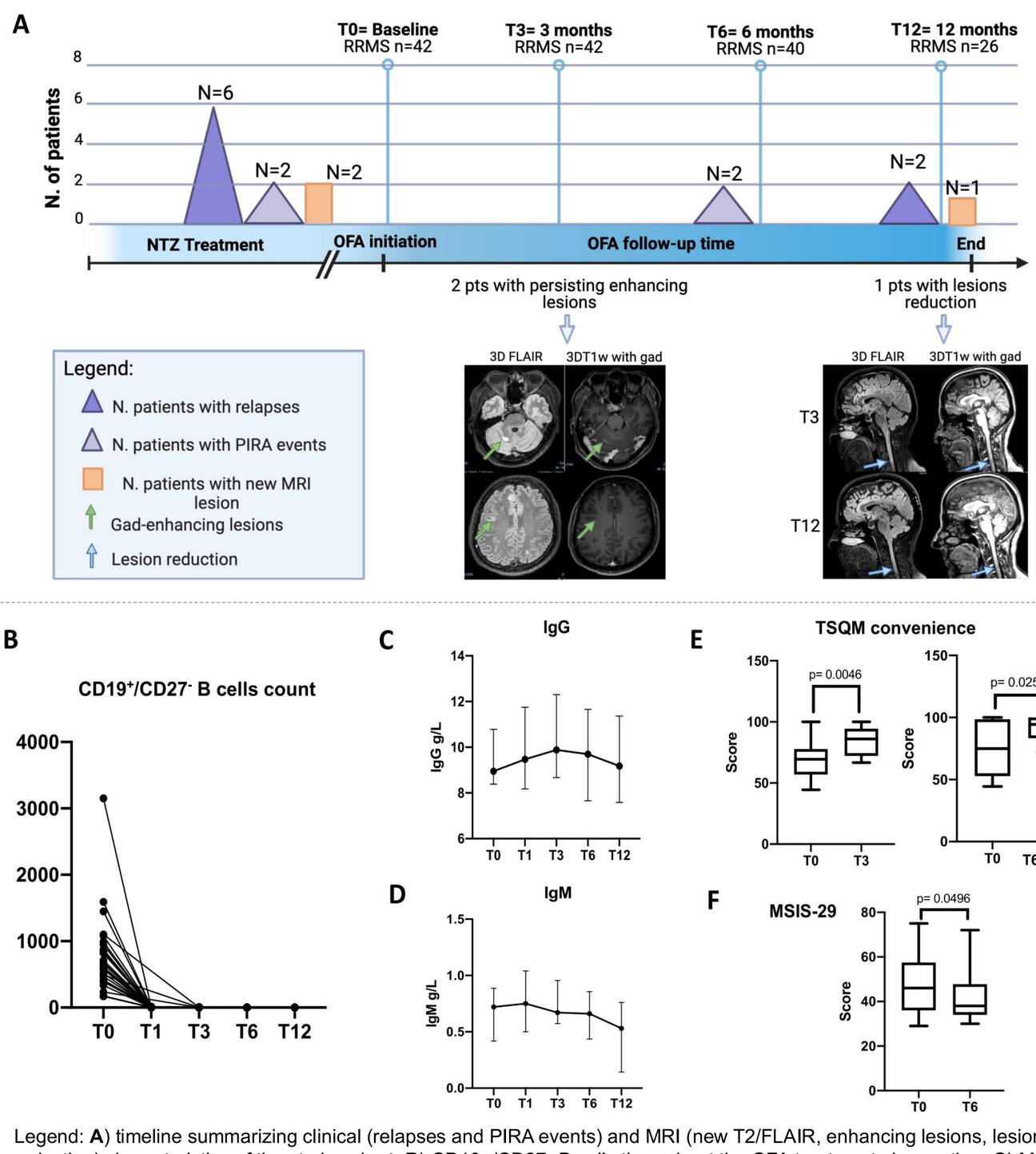
OFA was initiated in a mean of 38±12.2 days from NTZ discontinuation. By the 12-month, 15.4% of patients showed EDA. ARR at 12-months was not significantly different to ARR on NTZ (p= p=0.394). No patients showed rebound of disease activity, new PIRA, PML or severe infections events. Compared to baseline, TSQM convenience score was increased (p=0.005) at 3-months and MSIS-29 score was reduced at 6-months of OFA therapy (p=0.05).

RMS cohort switching from natalizumab to ofatumumab

	TOTAL COHORT	SWITCHING GROUPS		
Baseline clinical data	**N = 40**	**Safety N= 33**	**EDA= 9**	**p-value**
Age, years	38.3±10.1	37.7±10.1	40.4±10.4	0.470
Female	26 (69.1)	20 (60.6)	6 (66.7)	0.999
Disease duration, years	6 (1-19)	6 (1-19)	6 (2-18)	0.730
Last JCV index	1.94±1.1	2.14±1.0	1.11±0.99	0.016
ARR 1-year prior the switch to OFA	0.27±0.6	0.1±0.4	1.0±0.8	<0.0001
MRI activity 1-year prior the baseline	2 (4.8)	0	2 (22.2)	0.042
Previous therapies	2 (1-4)	2 (1-4)	2 (1-3)	0.657
Days from NTZ discontinuation to OFA	38±12.2	37.3±10.3	40.9±18.2	0.914
Duration of NTZ therapy, months	28.5 (6-134)	27 (24-134)	31 (6-68)	0.579
Disability (EDSS) at baseline	2 (0-7)	2 (0-6.5)	3 (1-5)	0.066
Follow-up, months	12 (4-25)	12 (5-25)	16 (4-24)	0.985
Prospective clinical data				
ARR at 12 months of OFA treatment	0.13 ± 0.3	0.09±0.28	0.25±0.5	0.439
New PIRA events	0	0	0	N/A
Severe adverse events (PML, infections)	0	0	0	N/A
New T2/FLAIR or gad enhancing lesions at T3	2 (5.7)	2 (5.55)	0	0.732
New T2/FLAIR or gad enhancing lesions at T12	1 (3.84) *	1 (4.76) °	0	0.836

Legend: ARR= annualized relapse rate; MRI=magnetic resonance imaging; NTZ=natalizumab; OFA=ofatumumab; EDSS= Expanded Disability Status Scale; PIRA= progression independent of relapse activity; PML=progressive multifocal leukoencephalopathy; FLAIR= fluid attenuated inversion recovery, EDA=evidence of disease activity on natalizumab treatment; N/A= not applicable
*26 patients were followed for 12 months
°21 patients were followed for 12-months

Most important findings of this prospective study on RMS switching from



Legend: **A**) timeline summarizing clinical (relapses and PIRA events) and MRI (new T2/FLAIR, enhancing lesions, lesions reduction) characteristics of the study cohort; **B**) CD19+/CD27- B cells throughout the OFA treatment observation; **C**) Median serum levels of IgG throughout the OFA treatment observation; **D**) Median serum levels of IgM throughout the OFA treatment observation; **E**) Boxplots showing TSQM score increase between T0 (NTZ) and T3 visit; **F**) Boxplots showing MSIS-29 score decrease between T0 (NTZ) and T6 visit

CONCLUSIONS

Ofatumumab (OFA) is a safe and effective alternative to NTZ for highly active MS patients at risk of PML. Additionally, OFA seems more convenient compared to NTZ.

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