Treatment failure rates in patients with neuromyelitis optica spectrum disorder included in an Argentinean registry

V. Tkachuk [1], P. López [2], L. Patrucco [3], J. Miguez [4], S. Liwacki [5], C. Vrech [6], N. Deri [7]J. Correale [8], M. Ysrraelit [8], F. Leguizamon [9], G. Luetic [10], M. Menichini [11], D. Tavolini [12], C. Mainella [13], G. Zanga [14], M. Burgos [15], J. Hryb [16], A. Barboza [17], R. Alonso [18], B. Silva [18], N. Fernández Liguori [19], A. Carrá [20], O. Garcea [18], J. Rojas [21]; Edgar Carnero contentti [2]

[1] Neuroimmunology Hospital de Clínicas "José de San Martín", [2] Neuroimmunology Hospital Alemán, [3] CEMBA Centro de Esclerosis Múltiple de Buenos Aires, [4] Enfermedades desmielinizantes Hospital Italiano Buenos Aires, [5] Clínica Reina Fabiola de Córdoba, [6] Servicio de Neurología - Hospital Córdoba, [7] Centro de Investigaciones Diabaid, CABA, [8] Departamento de Neurología - FLENI, Buenos Aires, [9] Hospital de Agudos, Dr. Teodoro Álvarez, Buenos Aires, [10] Instituto de Neurociencias de Rosario, Santa Fe, [11] Sanatorio Británico, Rosario, Santa Fe, [12] INECO Neurociencias Oroño, [13] Hospital Español de Rosario, Santa Fé, [14] Unidad Asistencial César Milstein Buenos Aires, [15] Servicio de Neurología - Hospital San Bernardo, Salta, [16] Servicio de Neurología - Hospital Carlos G. Durand, Buenos Aires, [17] Hospital Central de Mendoza, [18] CUEM Ramos Mejía de Buenos Aires, [19] Sanatorio Guemes de Buenos Aires, [20] Hospital Británico de Buenos Aires, [21] CEMIC, Buenos Aires

INTRODUCTION

Immunosuppressive therapies as azathioprine (AZA), mycophenolate mofetil (MMF) and rituximab (RTX) are widely used to prevent relapses in NMOSD. However, the rate of response to these classical therapies is unknown in Argentina. We aimed to describe and compare treatment failure rates in NMOSD (seropositive and seronegative for aquaporin-4 antibody) patients included in the Argentinean MS and NMOSD registry (RelevarEM, NCT 03375177).

METHODS

A retrospective cohort study was conducted in NMOSD patients included in RelevarEM (a nationwide, longitudinal, observational, non-mandatory registry of MS and NMOSD in Argentina). NMOSD patients were defined based on validated diagnostic criteria. Only NMOSD patients who received AZA or MMF for at least 6 months or RTX for at least 1 month were included. Patients who were receiving AZA, MMF, or RTX and then switched to another 1 of these 3 therapies were included if the above-mentioned criteria for each drug were fulfilled. Data on patient demographics, clinical and neuroradiological findings, and treatments administered were collected. Treatment failure was defined as any new attack/relapse that occurred despite immunosuppressive treatment.

Table 1. Demographic, clinical, and paraclinical characteristics according to treatments

	Initial treatment		
	Azathioprine N= 105	**Mycophenolate Mofetil N= 5**	**Rituximab N= 29**
Seropositive NMO (N=89)	66 (74.2)	5 (5.6)	18 (20.2)
Seronegative NMO (N=50)	39 (78)	0	11 (22%)
Mean follow up time, months	41 ± 16	44 ± 10	39± 8
Mean age at onset, y	41.3 ± 4.2	39.8 ± 3.7	40.6 ± 5.3
Median age (range), y	43.2 ± 5.4	45.3±4.2	44.3±6.3
Female sex	77 (73.3)	5 (100)	25 (86.2)
	2.5 (2-6)	3 (2-5.5)	3 (2-5.5)
Patients with activity during follow up, n (%)	45 (42.8)	2 (40)	3 (10.3)
Patients that change treatment during follow up, n (%)	49 (46.6)	2 (40)	4 (13.8)

Table 2. Predictors of failure in NMOSD patients according to Cox proportional hazards models

	Pre treatment ARR	Post treatment ARR	Change From Pretreatment to Posttreatment	Hazard Risk Relative to Rituximab (95% CI)	P value
Azathioprine	1.76 ±0.45	0.86 ±0.45	56%	1.67 (1.34-3.54)	0.01
MMF	1.88 ±0.54	0.97 ±0.78	48%	2.01 (1.86-4.43)	0.008
RTX	2.01 ±0.49	0.42 ±0.22	79%	1 [Reference]	-

RESULTS

We included 139 NMOSD patients received AZA (n=105), MMF (n=5) or RTX (n=29) with a mean follow-up time of 41.3 ± 11.4 months , and median of EDSS at treatment initiation of 3.

We observed a reduction in the annualized relapse rate from pre-treatment to post-treatment of 56%, 48%, and 79% respectively with a Hazard Risk relative to RTX (95% CI) of 1.67 (1.34-3.54, p=0.01) for AZA and 2.01 (1.86-4.43, p=0.008) for MMF.

AZA, MMF and RTX failure was observed in 45 (42.8%), 2 (40%) and 3 (10.3%) patients, respectively.

CONCLUSION

Treatment failure rates were higher for AZA and MMF than RTX in Argentinean NMOSD patients in a real-word setting.

The authors have no potential conflict of interest to disclose.

veronica.tkachuk@gmail.com