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POSTER PRESENTATION

The Real-world Efficacy and Safety of Off-label Rituximab in a Large Cohort of Middle Eastern Multiple Sclerosis Patients

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INTRODUCTION

- Rituximab, a monoclonal anti-CD20 antibody, has emerged as a potent off-label therapy for multiple sclerosis (MS), targeting B cells to reduce inflammation and disease activity.
- Its ability to deplete B cells has shown promise in both relapsing-remitting and progressive forms of MS.
- Despite being off-label for MS, rituximab's use has expanded globally due to its efficacy in reducing relapses, MRI activity, and disability progression.
- Real-world data on its efficacy and safety in Middle Eastern populations are limited.

AIM

- To investigate the efficacy and safety of rituximab in MS patients in clinical practice setting.

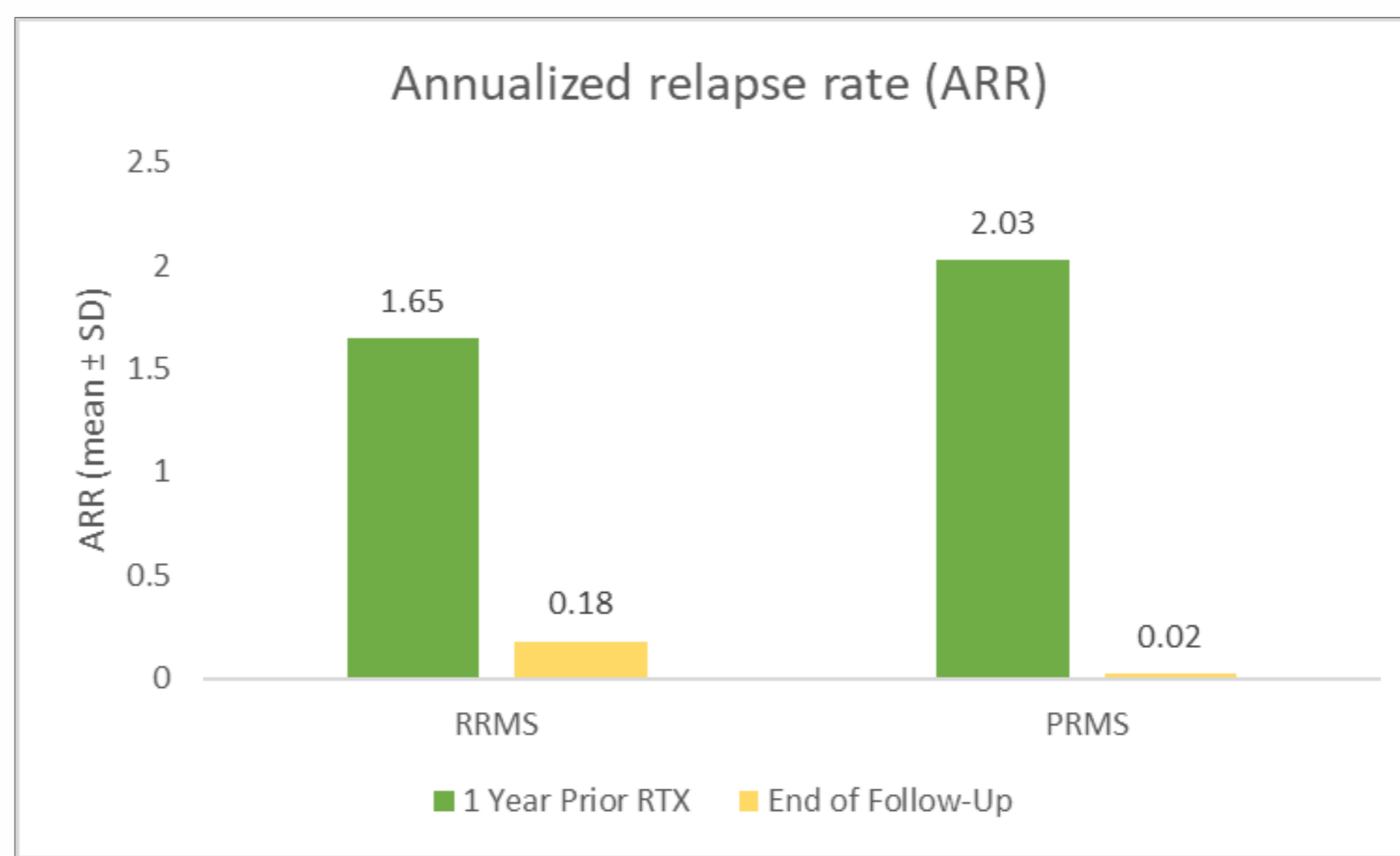
METHODS

- This is a multicenter, observational, retrospective study including MS patients ≥ 18 years of age with a confirmed diagnosis of MS, ever treated with at least 2 infusions of off-label rituximab, and followed for ≥ 6 months.
- Clinical data was collected from 7 Middle Eastern countries (Iraq, Kuwait, Lebanon, Oman, Saudi Arabia, Tunisia, and United Arab of Emirates) through an analysis of the MENACTRIMS registry.
- Relapses, disability worsening, and magnetic resonance imaging (MRI) activity data were collected from medical charts.
- No-evidence-of-disease-activity-3 (NEDA-3) status was assessed and tested for potential confounders.
- Safety outcomes were also recorded.

RESULTS

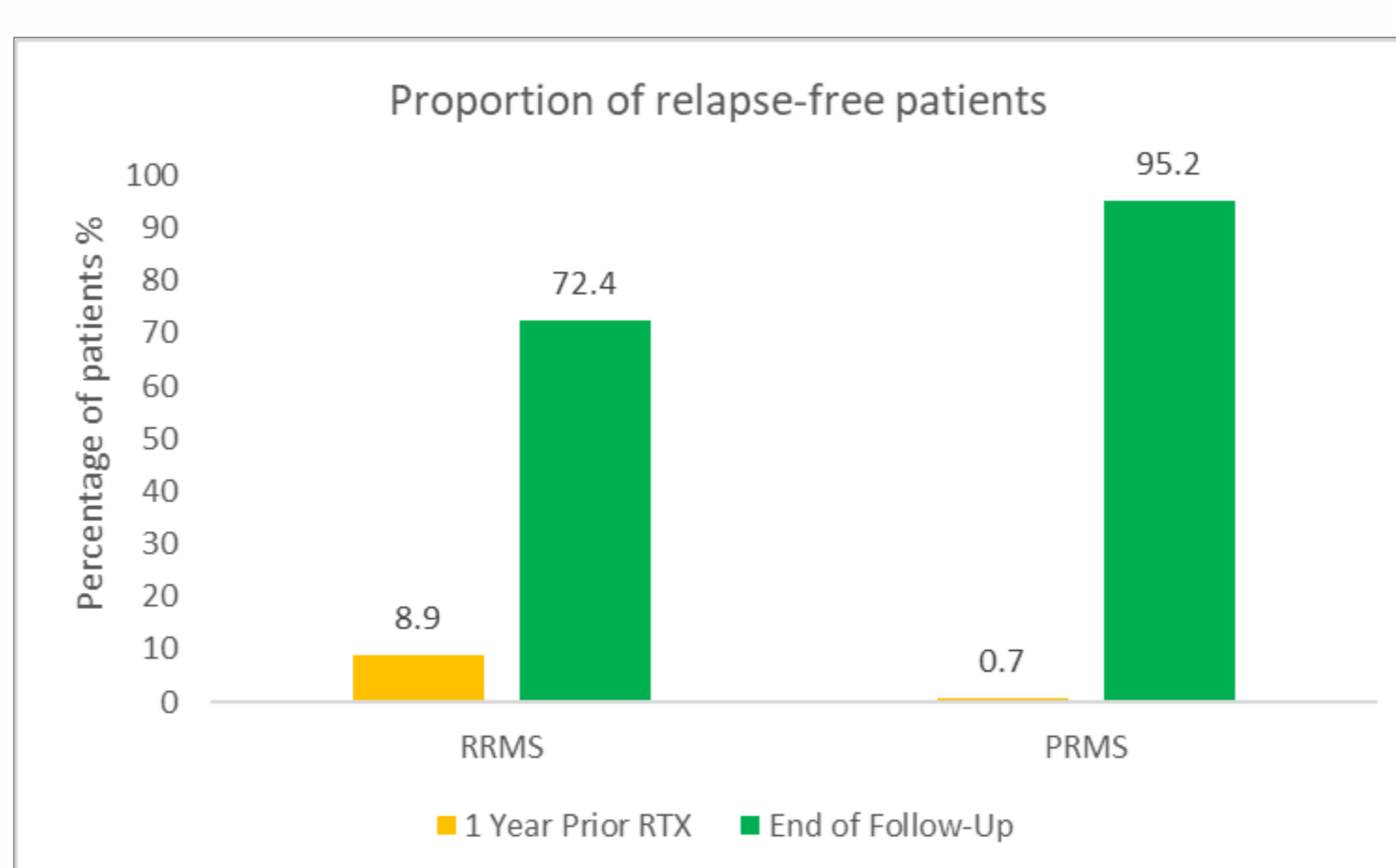
- A total of 774 MS patients treated with rituximab were included in the study: 482 relapsing-remitting MS (RRMS) and 292 progressive-relapsing MS (PRMS), also called active PMS. Treatment consisted of 500 mg or 1000 mg rituximab IV every 6–12 months. The cohort was predominantly female (72.1%), with a median follow-up of 2.0 (1.0-4.27) years.

Figure 1. Annualized relapse rate



- Rituximab shows a significant efficacy with 89.1 % and 99.0 % reduction in ARR in RRMS and PRMS, respectively.

Figure 2. Proportion of relapse-free patients



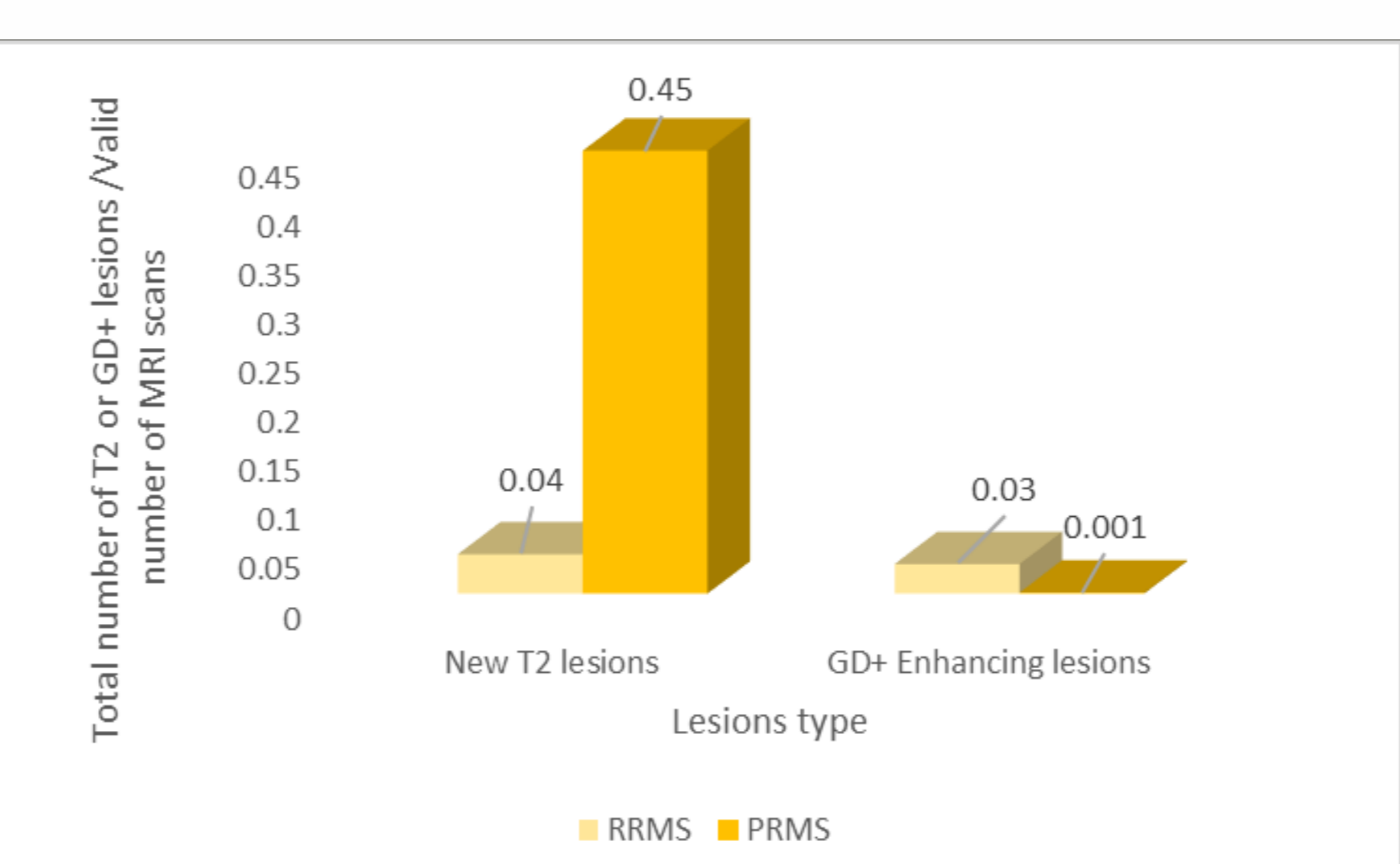
- At the end of follow-up, 72.4% of RRMS and 95.2% of PRMS patients were free of relapses.

Figure 3. Confirmed Disability Progression/Improvement in RRMS and PRMS



- The median (IQR) Expanded Disability Status Scale (EDSS) remained unchanged in RRMS (3.0 [1.5 – 4.0]), while it significantly increased by 1.0 in PRMS (p<0.001).
- The majority of RRMS patients (86.7 %) were free of disability worsening post RTX treatment.

Figure 4. MRI activity



- Post RTX treatment, 91.9% and 96.8% of RRMS, and 8.4% and 99.7 % of PRMS patients were free of T2 and GD+ enhancing lesions, respectively.
- At the end of follow-up period, no MRI activity was reported in 89.1% of RRMS compared to 8.1% of PRMS patients.

No Evidence of Disease Activity-3 (NEDA-3)

- NEDA-3 was achieved in 47.3% (166/351) of RRMS patients with available data.

Table 2. Multivariate logistic regression analysis for NEDA-3

Variables	NEDA-3		
	β	95% CI	p-value
Age	0.960	0.932 – 0.989	0.008
Type of MS	0.006	0.002 – 0.22	<0.001
Disease duration since symptoms onset	1.173	1.009 – 1.364	0.037
Treatment prior rituximab	0.124	0.048 – 0.321	<0.001
Number of relapses 1 year prior RTX	0.490	0.354 – 0.678	<0.001
Baseline EDSS	0.543	0.471 – 0.627	0.001

EDSS: expanded disability status scale, MS: multiple sclerosis, RTX: rituximab

- Being RRMS, younger age, naïve-treatment, having no relapses prior RTX, and lower baseline EDSS increase potential of achieving NEDA-3.

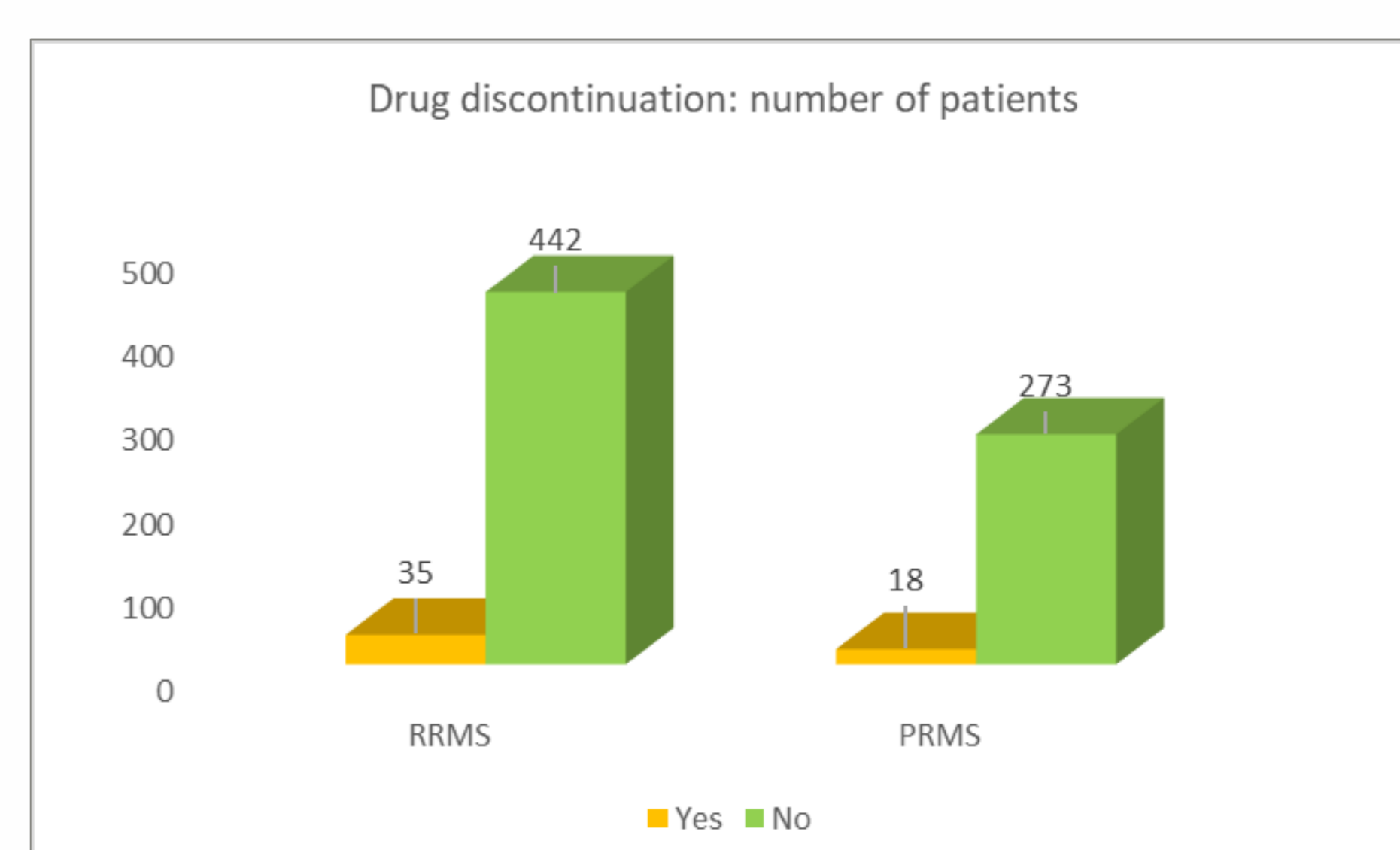
Table 3. Safety data

n (%)	RRMS	PRMS	Total
Any adverse event	218 (44.4)	273 (55.6)	491
Adverse events requiring hospitalization	3 (75.0)	1 (25.0)	4
Adverse event leading to discontinuation of drug	1 (100.0)	-	1
Adverse Events – Description			
• Infusion reactions	184 (84.4)	270 (98.8)	454 (92.4)
• Infections	23 (10.5)	1 (0.4)	24 (5.0)
• Depression	4 (1.8)	-	4 (0.8)
• Dermatological disorder	3 (1.3)	-	3 (0.6)
• Elevated liver enzymes	1 (0.5)	1 (0.4)	2 (0.4)
• Blood dyscrasia	1 (0.5)	-	1 (0.2)
• Thrombosis	-	1 (0.4)	1 (0.2)
• Malignancy	1 (0.5)	-	1 (0.2)
• Humoral immunodeficiency	1 (0.5)	-	1 (0.2)
Infusion reactions, severity			
• Mild	n=184	n=270	n=454
• Moderate	183 (99.5)	270 (100.0)	453 (99.8)
• Severe	1 (0.5)	-	1 (0.2)
Infusion reactions, at which dose			
• 1 st Dose	181 (98.4)	268 (99.2)	449 (98.9)
• 2 nd Dose	3 (1.6)	1 (0.4)	4 (0.9)
• 3 rd Dose	-	1 (0.4)	1 (0.2)

n: number of events

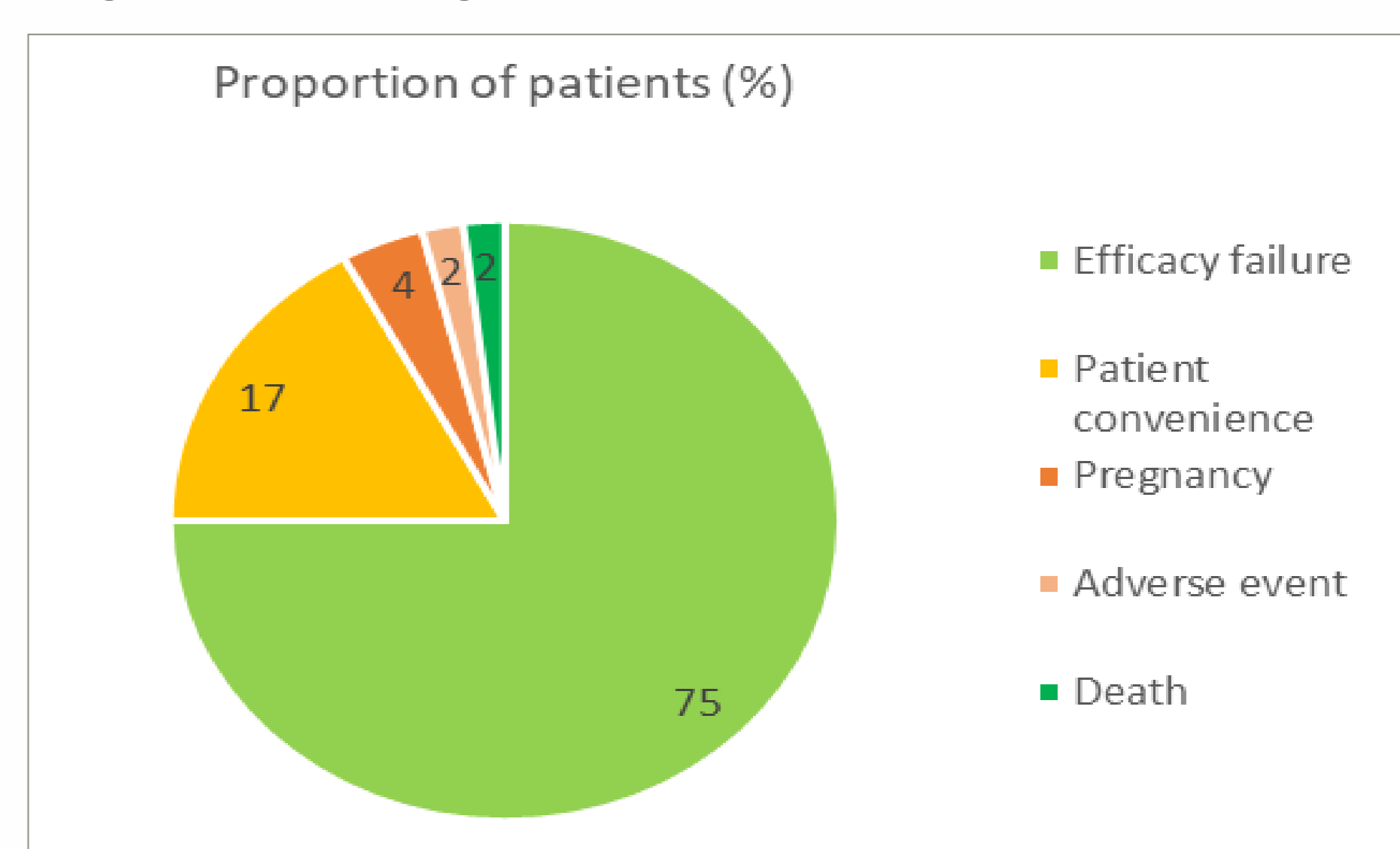
- A total of 491 AEs in 489 (217 RRMS and 272 PRMS) patients were reported.
- Primarily was the mild infusion-related reactions, with one moderate case.
- Only four patients experienced serious AEs requiring hospitalization.
- Progressive multifocal leukoencephalopathy was not detected in any of the patients.

Figure 5. Drug survival



- A total of 53/768 patients discontinued the treatment for any reason

Figure 6. Reason of drug discontinuation



- Drug survival**, defined as the proportion of patients who had not discontinued due to disease activity or AE (727/768) is **94.6 %**.

CONCLUSIONS

Our study findings are in line with results of other real-world and randomized clinical trials. Off-label rituximab demonstrated significant real-world efficacy by reducing relapses in both RRMS and PRMS patients, stabilizing disability and MRI findings in RRMS patients, and maintaining a well-tolerated safety profile.

Table 1. Clinical and demographic data of MS on RTX at baseline (N= 774).

Characteristics	RRMS (n=482)	PRMS (n=292)	Total (n=774)
Age, y, mean (SD)	38.6 (9.3)	41.2 (8.4)	39.6 (9.1)
• Age at symptoms onset, y, mean (SD)	27.2 (7.9)	28.3 (8.5)	27.6 (8.2)
Sex, n (%)			
• Female	342 (71.0)	216 (74.0)	558 (72.1)
Disease duration, y, mean (SD)			
• Since Symptoms onset	11.4 (6.5)	12.9 (5.8)	11.9 (6.3)
• Since Diagnosis	9.8 (5.8)	11.5 (5.3)	10.4 (5.7)
Baseline EDSS score, median (IQR)	3.0 (1.5-4.0)	6.0 (6.0-6.0)	4.0 (3.0-6.0)
Number of relapses 1 year prior RTX, mean (SD)	1.65 (0.87)	2.03 (0.61)	1.80 (0.81)
Relapses prior RTX, n (%)			
• 0	43 (8.9)	2 (0.7)	45 (5.8)
• 1	170 (35.3)	45 (15.4)	215 (27.7)
• 2	186 (38.6)	187 (64.0)	373 (48.2)
• 3	81 (16.8)	58 (19.9)	139 (18.0)
• 4	2 (0.4)	-	2 (0.3)
Proportion of patients with prior DMT use n (%)			
• Treatment naïve	92 (19.1)	7 (2.4)	99 (12.8)
• 1 previous DMT	270 (56.0)	223 (76.4)	493 (63.7)
• 2 previous DMTs	91 (18.9)	62 (21.2)	153 (19.8)
• 3 Previous DMTs	22 (4.6)	-	22 (2.8)
• 4 Previous DMTs	6 (1.2)	-	6 (0.8)
• 5 previous DMTs	1 (0.2)	-	1 (0.1)
Last DMT prior to RTX, n (%)	n= 390	n=285	n= 675
• IFN/GA	175 (44.9)	196 (68.8)	371 (55.0)
• Fingolimod	117 (30.0)	25 (8.8)	142 (21.0)
• Natalizumab	72 (18.4)	64 (22.4)	136 (20.2)
• Azathioprine / Mycophenolic acid	11 (2.8)	-	11 (1.61)
• DMF	7 (1.8)	-	7 (1.0)
• Plasmapheresis	3 (0.8)	-	3 (0.44)
• Alemtuzumab	2 (0.5)	-	2 (0.30)
• Teriflunomide	2 (0.5)	-	2 (0.30)
• Ocrelizumab	1 (0.3)	-	1 (0.15)
Reason for switching to RTX, n (%)	n= 390	n=285	n=675
• Inefficacy	249 (63.8)	185 (65.0)	434 (64.3)
• Positive JCV	74 (19.0)	50 (17.5)	124 (18.4)
• Approval restrictions	35 (9.0)	49 (17.2)	84 (12.44)
• Adverse events	17 (4.4)	-	17 (2.5)
• Personal preference	10 (2.6)	1 (0.3)	11 (1.62)
• Pregnancy planning	3 (0.7)	-	3 (0.44)
• Non-compliance	2 (0.5)	-	2 (0.3)
Maintenance Dose of RTX (mg), n (%)	n= 482	n= 292	n=774
• 500	13 (2.7)	1 (0.3)	14 (1.8)
• 1000	469 (97.3)	291 (99.7)	760 (98.2)
Dose frequency (months), n (%)			
• 6	476 (98.8)	292 (100.0)	768 (99.2)
• >6 and <12	4 (0.8)	-	4 (0.5)
• 12	2 (0.4)	-	2 (0.3)

DMF: dimethyl fumarate, DMT: disease-modifying therapy, EDSS: expanded disability status scale, GA: Glatiramer acetate, IFN: interferon, IQR: interquartile range, n: number, PRMS: progressive-relapsing multiple sclerosis, RTX: Rituximab, RRMS: relapsing-remitting multiple sclerosis, SD: standard deviation