



HAL
open science

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

Ghida Ismail, Maya Zeineddine, Raed Al-Roughani, Samar Farouk, Akram Al-Mahdawi, Samia Khoury, Jihad Inshasi, Jaber Al-Khabouri, Abdullah Al-Asmi, Riadh Gouider, et al.

► **To cite this version:**

Ghida Ismail, Maya Zeineddine, Raed Al-Roughani, Samar Farouk, Akram Al-Mahdawi, et al.. The Real-world Efficacy and Safety of Off-label Rituximab in a Large Cohort of Middle Eastern Multiple Sclerosis Patients. 9th MENACTRIMS CONGRES, Nov 2024, JEDDAH, Saudi Arabia. hal-04835961

HAL Id: hal-04835961

<https://unilim.hal.science/hal-04835961v1>

Submitted on 13 Dec 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



POSTER PRESENTATION

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

Ghida Ismail¹, Maya Zeineddine^{1,2}, Raed Al-Roughani³, Samar Farouk Ahmed⁴, Akram Al-Mahdawi⁵, Samia Khoury⁶, Nabil El-Ayoubi⁶, Jihad Inshasi⁷, Jaber Al-Khabouri⁸, Abdullah Al-Asmi⁹, Riadh Gouider¹⁰, Salman Aljarallah¹¹, Nuha Alkawahjah¹¹, Yaser Al Malik^{12,13,14}, Ahmad Abulaban^{12,15}, Seraj Makkawi^{12,15,16}, Osama Khojah^{12,15,16}, Taghrid El-Hajji¹⁷, Joelle Massouh¹⁸, Husam ALSalamat¹⁹, Hani Dimassi², Amal Al-Hajje^{20,21}, Pascale Salameh^{20,21,22,23}, Farid Boumediene², Bassem Yamout¹⁸

¹Inserm U1094, IRD U270, Univ. Limoges, CHU Limoges, EpiMACT - Epidemiology of chronic diseases in tropical zone, Institute of Epidemiology and Tropical Neurology, Omega Health, Limoges, France, ²School of Pharmacy, Lebanese American University, Byblos, Lebanon, ³Amiri Hospital, Kuwait, Kuwait, ⁴Ibn Sina Hospital, Kuwait, Kuwait, ⁵Baghdad Medical City Teaching Hospital, Baghdad, Iraq, ⁶American University of Beirut Medical Center, Nehme and Therese Tohme Multiple Sclerosis Center, Beirut, Lebanon, ⁷MS Department, Rashid Hospital and Dubai Medical College, Dubai Health Authority, Dubai, United Arab Emirates, ⁸Department of Neurology, The Royal Hospital, Muscat, Oman, ⁹Neurology Unit, Department of Medicine, College of Medicine and Health Sciences and Sultan Qaboos University Hospital, Sultan Qaboos University, Muscat, Oman, ¹⁰Department of Neurology, LR185SP03, Clinical Investigation Center "Neurosciences and Mental Health"- Razi University Hospital- Mannouba, Tunis, Tunisia, ¹¹King Saud University, King Saud University Medical City, Riyadh, Saudi Arabia, ¹²College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia, ¹³King Abdullah International Medical Research Center, Riyadh, Saudi Arabia, ¹⁴Neurology Department, King Abdulaziz Medical City, Riyadh, Saudi Arabia, ¹⁵Department of Neurology, Ministry of the National Guard-Health Affairs, Jeddah, Saudi Arabia, ¹⁶King Abdullah International Medical Research Center, Jeddah, Saudi Arabia, ¹⁷Faculty of Medical Sciences, Lebanese University, Beirut, Lebanon, ¹⁸Neurology Institute, Harley Street Medical Centre, Abu Dhabi, United Arab Emirates, ¹⁹Faculty of Medicine, Al-Balqa Applied University, Al-Salt 19117, Jordan, ²⁰Faculty of Pharmacy, Lebanese University, Beirut, Lebanon, ²¹National Institute of Public Health, Clinical Epidemiology and Toxicology (INSPECT-LB), Beirut, Lebanon, ²²School of Medicine, Lebanese American University, Byblos, Lebanon, ²³Department of Primary Care and Population Health, University of Nicosia Medical School, 2417, Nicosia, Cyprus

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.

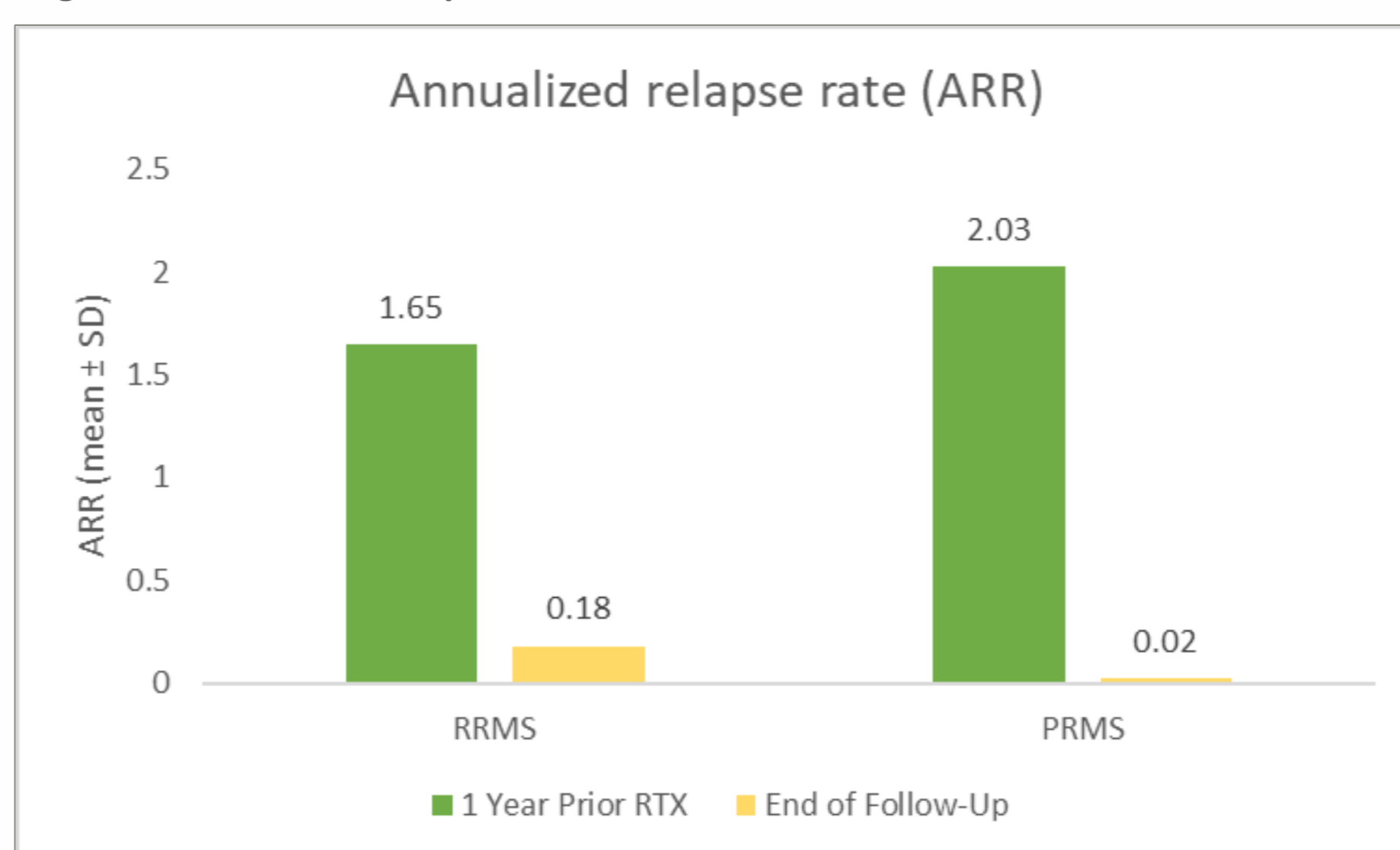
METHODS

- 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

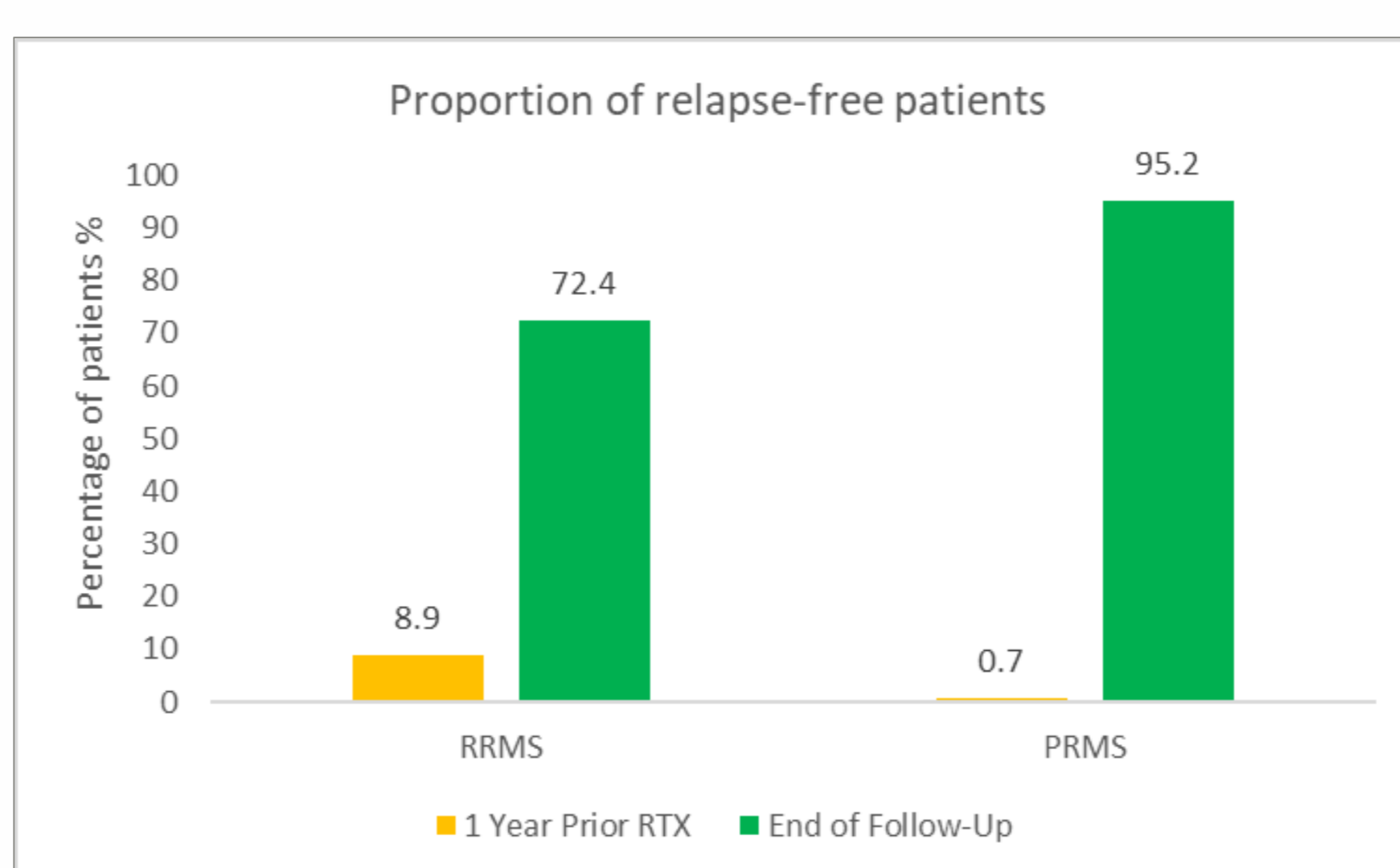
- A total of 774 MS patients treated with rituximab were included in the study: 482 relapsing-remitting MS (RRMS) and 292 progressive-relapsing MS (PRMS), also called active PMS. Treatment consisted of 500 mg or 1000 mg rituximab IV every 6–12 months. The cohort was predominantly female (72.1%), with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



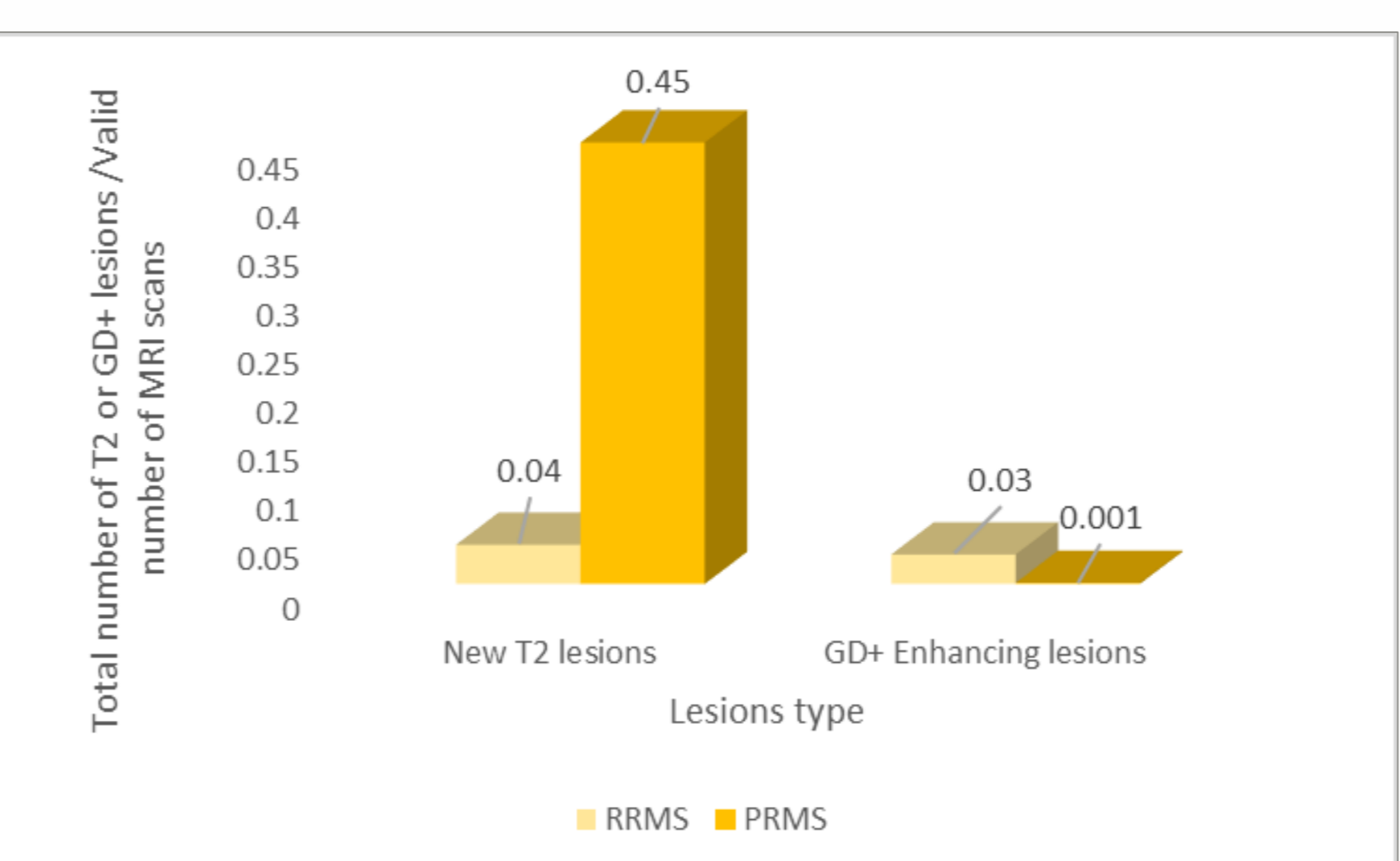
- At the end of follow-up, 72.4% of RRMS and 95.2% of PRMS patients were free of relapses.

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.

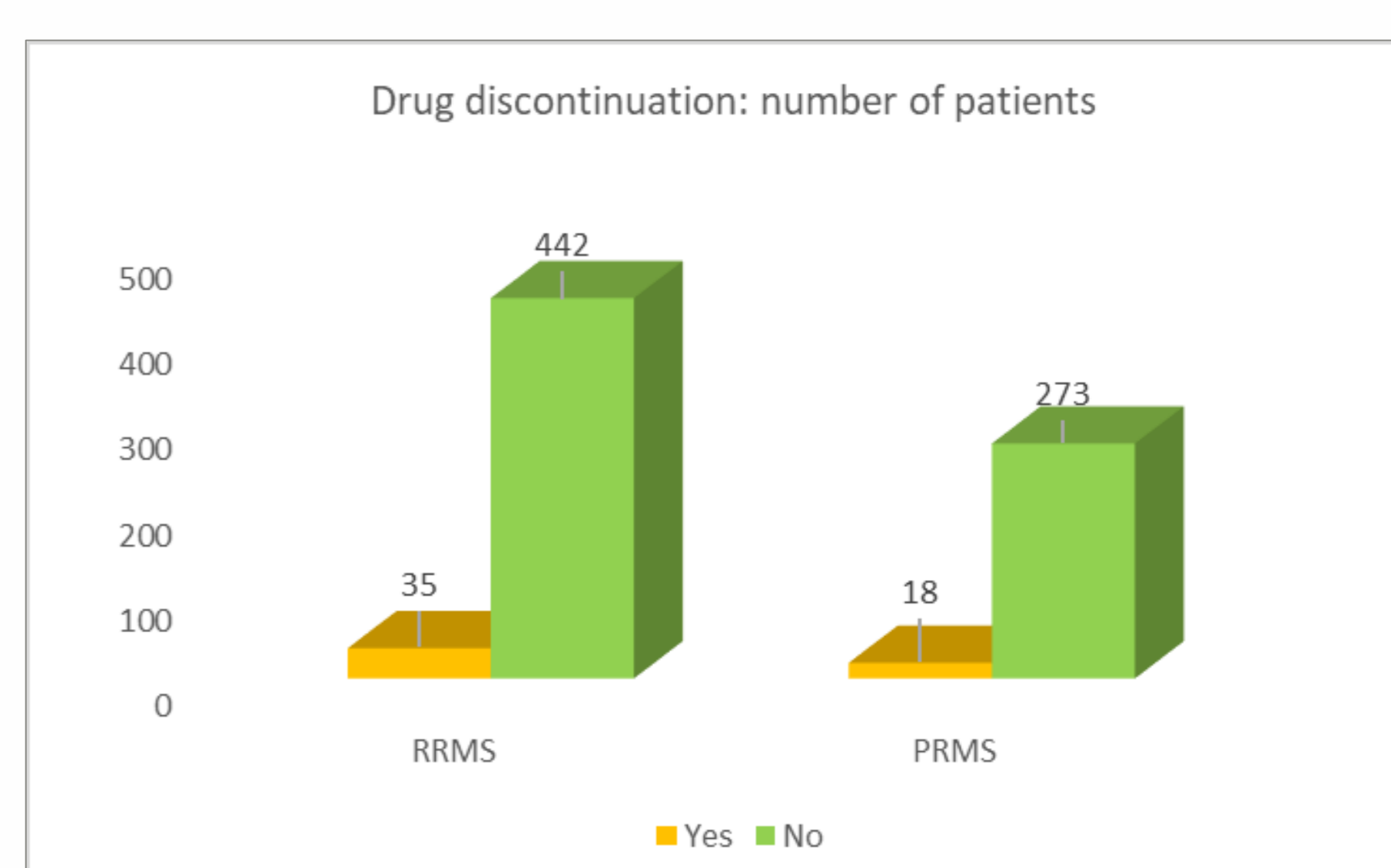
Table 3. Safety data

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

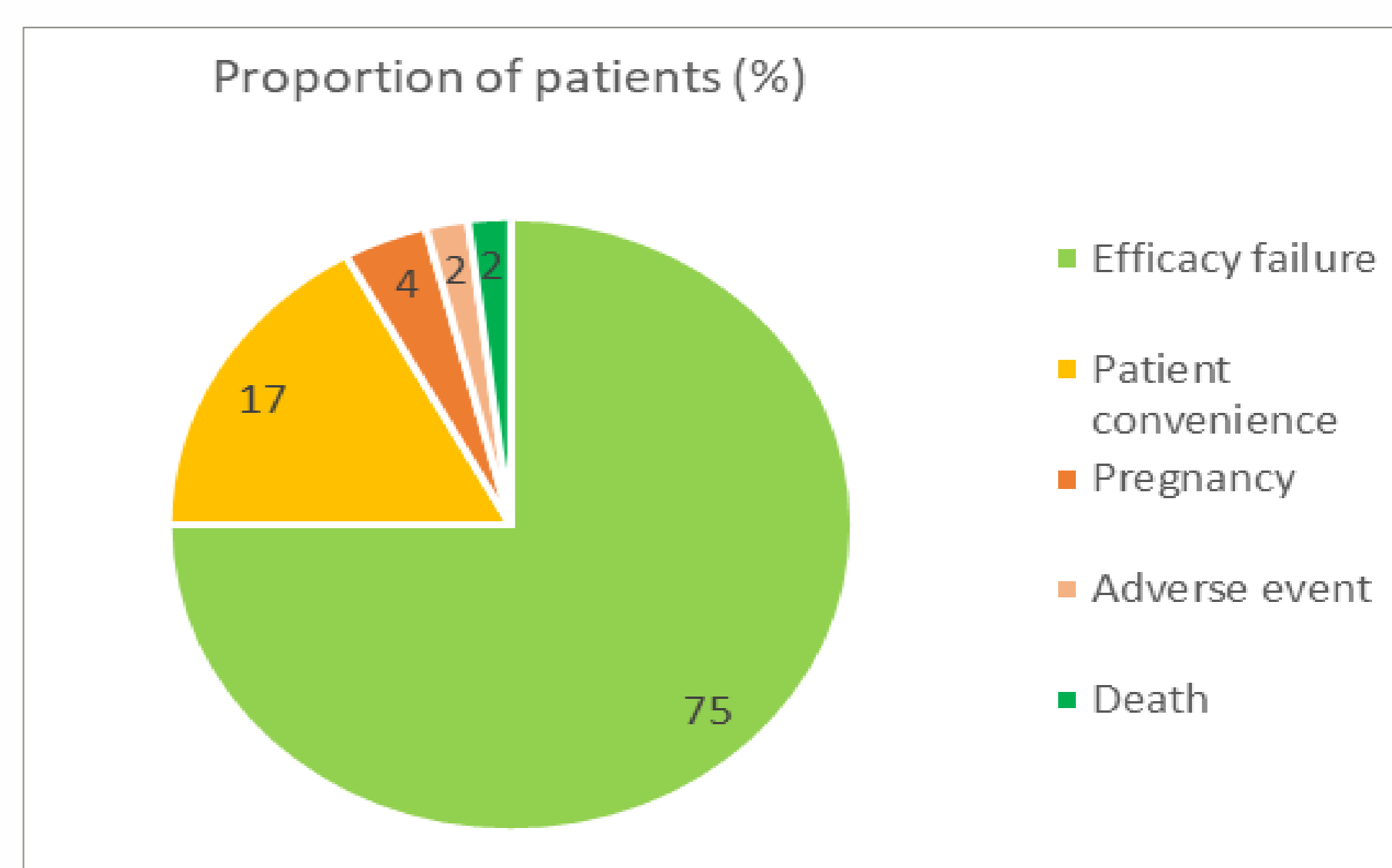
- A total of 491 AEs in 489 (217 RRMS and 272 PRMS) patients were reported.
- Primarily was the mild infusion-related reactions, with one moderate case.
- Only four patients experienced serious AEs requiring hospitalization.
- Progressive multifocal leukoencephalopathy was not detected in any of the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