SUPPLEMENTARY MATERIAL

Real-world persistence with ocrelizumab in multiple sclerosis: a systematic review

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Appendix A. Search terms used

Medline

Searched 07/10/22 via OvidSP interface.

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to October 06, 2022>

Search Strategy:

1 Multiple Sclerosis, Relapsing-Remitting/ (7781)

2 Multiple Sclerosis, Chronic Progressive/ (2512)

3 ((("chariot disease" or ((disseminated or insular or multiple$) adj1 sclerosis) or "encephalomyelitis disseminata" or MS) adj2 (relaps$ or remission$ or remitting or progression$ or progressive)) or RRMS or PPMS).ti,ab. (16679)

4 or/1-3 (19061)

5 exp "Treatment Adherence and Compliance"/ (271360)

6 (abstain$ or abstinence$ or adher$ or nonadher$ or cessati$ or comply$ or compliance or noncompliance or continu$ or discontinu$ or persist$ or withdraw$ or withhold$).ti,ab. (2320881)

7 5 or 6 (2509450)

8 (ocrelizumab or Ocrevus$ or PR070769 or PRO-70769 or PRO70769 or "rhuMAb 2H7" or RO4964913).af. (767)

9 Epidemiologic studies/ (9177)

10 exp case control studies/ (1358762)

11 exp cohort studies/ (2401679)

12 Case control.tw. (146929)

13 (cohort adj (study or studies)).tw. (287049)

14 Cohort analy$.tw. (10812)

15 (Follow up adj (study or studies)).tw. (54510)

16 (observational adj (study or studies)).tw. (146913)

17 Longitudinal.tw. (302066)

18 Retrospective.tw. (689382)

19 Cross sectional.tw. (470577)

20 Cross-sectional studies/ (442017)

21 or/9-20 (3615694)

22 4 and 7 and 8 and 21 (30)

Embase

Searched 07/10/22 via OvidSP interface.

Database: Embase <1974 to 2022 Week 39>

Search Strategy:

1 multiple sclerosis/ (148306)

2 ((("chariot disease" or ((disseminated or insular or multiple$) adj1 sclerosis) or "encephalomyelitis disseminata" or MS) adj2 (relaps$ or remission$ or remitting or progression$ or progressive)) or RRMS or PPMS).ti,ab. (34884)

3 1 or 2 (151192)

4 exp patient compliance/ (180262)

5 exp treatment withdrawal/ (255325)

6 (abstain$ or abstinence$ or adher$ or nonadher$ or cessati$ or comply$ or compliance or noncompliance or continu$ or discontinu$ or persist$ or withdraw$ or withhold$).ti,ab. (3184794)

7 or/4-6 (3382776)

8 ocrelizumab/ (3311)

9 (ocrelizumab or Ocrevus$ or PR070769 or PRO-70769 or PRO70769 or "rhuMAb 2H7" or RO4964913).af. (3444)

10 8 or 9 (3444)

11 Clinical study/ (160539)

12 Case control study/ (193371)

13 Family study/ (25694)

14 Longitudinal study/ (178980)

15 Retrospective study/ (1314578)

16 Prospective study/ (798085)

17 Randomized controlled trials/ (235539)

18 16 not 17 (788668)

19 Cohort analysis/ (901142)

20 (Cohort adj (study or studies)).mp. (422529)

21 (Case control adj (study or studies)).ti,ab. (158099)

22 (follow up adj (study or studies)).ti,ab. (70450)

23 (observational adj (study or studies)).ti,ab. (227238)

24 (epidemiologic$ adj (study or studies)).ti,ab. (117592)

25 (cross sectional adj (study or studies)).ti,ab. (303153)

26 or/11-15,18-25 (3569355)

27 3 and 7 and 10 and 26 (221)

Appendix B. PICOS criteria

Element	Inclusion Criteria	Exclusion criteria
Population	• Patients with relapsing remitting multiple sclerosis (RRMS) or primary progressive multiple sclerosis (PPMS)	• Studies not specifically reporting on the population specified in the inclusion criteria
Intervention	• Ocrelizumab	• NA
Comparator(s)	• Any/none	• NA
Outcome(s)	• Any relating to discontinuation, persistence, adherence, or compliance	• Outcomes not listed in this section
Study type(s)	• Observational/real-world evidence studies (prospective/retrospective cohort, cross sectional, case control, case series) of sufficient sample size (e.g., ≥ 10 patients) • Any country • English language studies	• Studies not reporting real-world evidence (e.g., RCTs, cost-effectiveness models) • Non-English language studies

Table S1. Overview of study characteristics

Author (year of publication)	Full text/abstract	Country	Total sample size	Type of MS	Sample size by type of MS	Line of ocrelizumab treatment		Exposure time
						First line	Switch	
Relapsing remitting MS (RRMS)								
Bewick (2020)	Abstract	England	28	RRMS	28	✓	✓	NR
Bossart (2022)	Full text	Switzerland	668	RRMS	668	NR	NR	6 months
Evertsson (2020)	Full text	Sweden, USA	472	RRMS	472	✓	✓	NR
Frahm (2022)	Full text	Germany	2536	RRMS	2536	×	✓	NR
Garcia-Canibano (2021)	Full text	Qatar	57	RRMS	57	✓	✓	19 months (median)
Smoot (2019)	Abstract	USA	21	RRMS	21	×	✓	NR
Zanghi (2021)	Full text	Italy	120	RRMS	120	×	✓	6-18 months
Zivadinov (2022)	Full text	USA	27	RRMS	27	×	✓	24 months
Primary progressive MS (PPMS)								
Braune (2021)	Abstract	Germany	460	PPMS	460	NR	NR	1.5 years (mean)
Lopez Ruiz (2020)	Abstract	Spain	18	PPMS	18	✓	✓	13.8 months (mean)
Relapsing remitting and primary progressive MS (stratified)								
Braune (2020)	Abstract	Germany	439	RRMS	352	✓	✓	≥3 months
				PPMS	52	✓	✓	
				SPMS	35	✓	✓	
Butzkueven (2019)	Abstract	Europe and Australia	1216	RRMS	882	✓	✓	≥6 months
				PPMS	174	✓	✓	
				SPMS	160	✓	✓	
Cellerino (2021)	Full text	Italy	153	RRMS	93	✓	✓	NR
				PPMS/SPMS	60	✓	✓	
Ellwardt (2020)	Full text	Germany	210	PPMS	55	✓	✓	NR

Author (year of publication)	Full text/abstract	Country	Total sample size	Type of MS	Sample size by type of MS	Line of ocrelizumab treatment		Exposure time
						First line	Switch	
				RRMS/SPMS	155	✓	✓	
Ozakbas (2021)	Abstract	NR	304	RRMS	87	NR	NR	6 months
				PPMS	42	NR	NR	
Rojas (2021)	Full text	Argentina, Chile, Mexico	81	RRMS	52	✓	✓	NR
				PPMS	29	✓	✓	
Weber (2022)	Full text	Germany	2100	RRMS	1702	✓	✓	1.03 years (mean)
				PPMS	398	✓	✓	1.06 years (mean)
Relapsing remitting and primary progressive MS (not stratified)								
Baghestani (2020)	Abstract	UAE	27	RRMS	22	✓	✓	NR
				PPMS	5	✓	✓	
Butzkueven (2021)	Abstract	Australia, Turkey, Kuwait, Belgium	800	RRMS	NR	✓	✓	1.8 years (median)
				PPMS	NR	✓	✓	
				SPMS	NR	✓	✓	
Coban (2021)	Full text	USA	82	RRMS	59	✓	✓	NR
				PPMS	14	✓	✓	
				SPMS	9	✓	✓	
Fernandez-Diaz (2021)	Full text	Spain	228	RRMS	144	✓	✓	12 months
				PPMS	59	✓	✓	
				SPMS	25	✓	✓	
Finder (2020)	Abstract	USA	178	RRMS	144	NR	NR	NR
				PPMS	NR	NR	NR	
				SPMS	NR	NR	NR	
Luxenberg (2021)	Abstract	USA	59	RRMS/PPMS	59	NR	NR	NR
Magyari (2020)	Abstract	Denmark	851	RRMS	735	✓	✓	0.9 years (median)
				PPMS	55	✓	✓	
				SPMS	61	✓	✓	
Pontieri (2022)	Full text	Denmark	1104	RRMS	946	✓	✓	NR
				PPMS	61	✓	✓	

Author (year of publication)	Full text/abstract	Country	Total sample size	Type of MS	Sample size by type of MS	Line of ocrelizumab treatment		Exposure time
						First line	Switch	
				SPMS	97	✓	✓	
Sempere (2020)	Full text	Spain	70	RRMS	49	NR	NR	NR
				PPMS	21	NR	NR	
Smoot (2022)	Abstract	USA	509	RRMS	421	NR	NR	34.3 months (median)
				PPMS	34	NR	NR	
				SPMS	54	NR	NR	
Tsantes (2020)	Abstract	Italy	23	RRMS	17	×	✓	15 months
				PPMS	6	×	✓	
Vollmer (2021)	Abstract	USA	245	RRMS	200	NR	NR	NR
				PPMS	8	NR	NR	
				SPMS	37	NR	NR	
Vollmer (2019)	Abstract	USA	357	RRMS	267	NR	NR	Up to 1 year
				PPMS	31	NR	NR	
				SPMS	59	NR	NR	

Abbreviations: MS, multiple sclerosis; NR, not reported; PPMS, primary progressive multiple sclerosis; RRMS, relapsing remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis

Table S2. Overview of baseline characteristics

Author (year)	Country	Intervention	Sample size	Age (years)	Disease duration (years)	No previous therapy, n (%)	ARR	EDSS
Relapsing remitting MS (RRMS)								
Bewick (2020)	England	Ocrelizumab	28	41.7 (mean) 25-28 (range)	NR	12 (42.8%)	NR	2 (median) 0-6 (range)
Bossart (2022)	Switzerland	Fingolimod	139	46.1 (mean) 9.9 (SD)	9.7 (mean) 6.4 (SD)	7 (5%)	NR	NR
		Dimethyl fumarate	104	44 (mean) 11.5 (SD)	8.6 (mean) 8.0 (SD)	13 (12.5%)	NR	NR
		Ocrelizumab	98	43.9 (mean) 11.9 (SD)	9.8 (mean) 6.7 (SD)	23 (24%)	NR	NR
		Natalizumab	44	42.9 (mean) 11.9 (SD)	11.8 (mean) 7.0 (SD)	6 (14%)	NR	NR
		Teriflunomide	31	50.9 (mean) 9.8 (SD)	9.7 (mean) 8.2 (SD)	4 (13%)	NR	NR
Cellerino (2021)	Italy	Ocrelizumab	93	36.9 (mean) 10.2 (SD)	9.3 (mean) 9.2(SD)	NR	0.8 (mean) 0.7 (SD)	2 (median) 2-3.5 (IQR)
Coban (2021)	US	Ocrelizumab	59	38 (mean) 11 (SD)	7.6 (mean) 9.8 (SD)	25 (42%)	1.4 (mean) 0.9 (SD)	2.2 (mean) 1 (SD)
Evertsson (2020)	Sweden and USA	Ocrelizumab	161	49.8 (mean) 11.9 (SD)	12.5 (mean) 8.32 (SD)	7 (4.3%)	NR	NR
		Rituximab	311	44 (mean) 11.7 (SD)	11.3 (mean) 8.9 (SD)	80 (25.7%)	NR	NR
Fernandez-Diaz (2021)	Spain	Ocrelizumab	144	39.5 (mean)	7.3 (mean) 6.6 (SD)	36 (25%)	1.12 (mean) 0.77 (SD)	2.8 (mean) 1.6 (SD)
Frahm (2022)	Germany	Ocrelizumab	178	41.8 (mean) 10.3 (SD)	NR	0	0.32 (NR)	3.5 (median)

Author (year)	Country	Intervention	Sample size	Age (years)	Disease duration (years)	No previous therapy, n (%)	ARR	EDSS
Garcia-Canibano (2021)	Qatar	Ocrelizumab	57	34.9 (mean) 10.4 (SD)	7.0 (mean) 6.6 (SD)	24 (38%)	NR	2.1 (mean) 2.4 (SD)
Ozakbas (2021)	NR	Ocrelizumab	87	NR	17.7 (mean)	NR	NR	NR
Pontieri (2022)	Denmark	Ocrelizumab	946	41.4 (mean) 10.2 (SD)	10.8 (mean) 8.2 (SD)	118 (12.5%)	0.6 (mean) 0.8 (SD)	2.9 (mean) 1.7 (SD)
Sempere (2020)	Spain	Ocrelizumab	49	39.2 (mean) 10.9 (SD)	7.7 (mean) 6.7 (SD)	10 (20%)	1.3 (mean) 0.65 (SD)	2.5 (median) 2-3 (IQR)
Smoot (2019)	USA	Ocrelizumab	21	43.7 (mean) 10.6 (SD)	NR	0	NR	3.4 (mean) 1.5 (SD)
Weber (2022)	Germany	Ocrelizumab	1702	41.6 (mean) 11.2 (SD)	9.0 (mean) 7.8 (SD)	294 (17.3%)	NR	3.18 (mean) 1.87 (SD)
Zanghi (2021)	Italy	Ocrelizumab	64	NR	NR	0	NR	3 (median) 2-4.5 (IQR)
		Rituximab	36	NR	NR	0	NR	4 (median) 2-4.5 (IQR)
		Cladribine	20	NR	NR	0	NR	2 (median) 1-3 (IQR)
Zivadinov (2022)	USA	Ocrelizumab	27	42.3 (mean) 10.6 (SD)	10.1 (mean) 5.6 (SD)	0	1.0 (median) 0.0-2.0 (IQR)	2.0 (median) 1.5-3.5 (IQR)
Primary progressive MS (PPMS)								
Braune (2021)	Germany	Any	460	62.29 (mean) 11.35 (SD)	18.7 (mean) 11.0 (SD)	NR	NR	NR
		Ocrelizumab	82	51.5 (mean) 10.03 (SD)	8.7 (mean) 7.8 (SD)	NR	NR	NR
Cellerino (2021)	Italy	Ocrelizumab	43	49.2 (mean) 8.6 (SD)	8.4 (mean) 6.5 (SD)	NR	NR	5.5 (median) 3.5-6.5 (IQR)

Author (year)	Country	Intervention	Sample size	Age (years)	Disease duration (years)	No previous therapy, n (%)	ARR	EDSS
Coban (2021)	US	Ocrelizumab	14	46 (mean) 10 (SD)	3.5 (mean) 3.7 (SD)	11 (79%)	NR	4.6 (mean) 1.5 (SD)
Fernandez-Diaz (2021)	Spain	Ocrelizumab	59	48.4 (mean) 9.3 (SD)	4.2 (mean) 4.9 (SD)	46 (78%)	NR	4.75 (mean) 1.43 (SD)
Lopez Ruiz (2020)	Spain	Ocrelizumab	18	47 (NR) 37-57 (NR)	5.4 (mean) 0.5-12.3 (NR)	12 (67%)	NR	5.7 (mean)
Ozakbas (2021)	NR	Ocrelizumab	42	NR	17.7 (mean)	NR	NR	NR
Pontieri (2022)	Denmark	Ocrelizumab	61	44.5 (mean) 6.9 (SD)	6.6 (mean) 3.7 (SD)	48 (79%)	0.1 (mean) 0.2 (SD)	4 (mean) 1.6 (SD)
Sempere (2020)	Spain	Ocrelizumab	21	47.1 (mean) 10.5 (SD)	2.8 (mean) 4.1 (SD)	19 (90%)	NR	3 (median) 3-4.8 (IQR)
Weber (2022)	Germany	Ocrelizumab	398	51.0 (mean) 9.9 (SD)	5.6 (mean) 6.8 (SD)	268 (67.3%)	NR	4.41 (mean) 1.59 (SD)
Relapsing remitting MS and primary progressive MS combined population[a]								
Baghestani (2020)	UAE	Ocrelizumab	26	40 (mean)	4.8 (mean) 0-12 (range)	6 (23%)	NR	NR
Braune (2020)	Germany	Ocrelizumab	439	NR	NR	NR	NR	NR
Butzkueven (2021)	Australia, Turkey, Kuwait, Belgium	Ocrelizumab	800	42.7 (median) 35.2-50.4 (IQR)	12.4 (mean) 8.3 (SD)	104 (13%)	NR	NR
Butzkueven (2019)	Europe & Australia	Ocrelizumab	1216	NR	NR	204 (16.8%)	NR	NR
Cellerino (2021)	Italy	Ocrelizumab	153	41.9 (mean) 11.4 (SD)	16.1 (mean) 9.9 (SD)	NR	0.5 (mean) 0.7 (SD)	3.5 (median) 2-5.5 (IQR)
Coban (2021)	US	Ocrelizumab	82	40 (mean)	8.0 (mean)	39 (47%)	1.4 (mean) 0.9 (SD)	3.1 (mean) 1.8 (SD)
Ellwardt (2020)	Germany	Ocrelizumab	210	42.1 (mean)	7.2 (mean)	50 (24%)	NR	3.9 (mean)

Author (year)	Country	Intervention	Sample size	Age (years)	Disease duration (years)	No previous therapy, n (%)	ARR	EDSS
Fernandez-Diaz (2021)	Spain	Ocrelizumab	228	42.7 (mean) 11.2 (SD)	6.98 (mean) 6.66 (SD)	83 (36.4%)	1.11 (mean) 0.81 (SD)	3.58 (mean) 1.83 (SD)
Finder (2020)	USA	Ocrelizumab	55	NR	NR	69 (38.8%)	NR	NR
		Fingolimod	NR	NR	NR	NR	NR	NR
		Dimethyl fumarate	NR	NR	NR	NR	NR	NR
		Teriflunomide	NR	NR	NR	NR	NR	NR
Luxenberg (2021)	USA	Ocrelizumab	59	59-84 (range)	NR	NR	NR	NR
Magyari (2020)	Denmark	Ocrelizumab	851	NR	NR	131 (15.4%)	NR	NR
Rojas (2021)	Argentina, Chile, Mexico	Ocrelizumab	81	41.3 (mean) 12 (SD)	8.4 (mean) 6.3 (SD)	29 (24%)	1.3 (mean) 0.6 (SD)	3.1 (mean) 1.8 (SD)
Sempere (2020)	Spain	Ocrelizumab	70	41.6 (mean)	6.53 (mean)	29 (41%)	NR	NR
Smoot (2022)	USA	Ocrelizumab	509	52.1 (mean) 12.6 (SD)	NR	NR	0.32 (mean)	NR
Tsantes (2020)	Italy	Ocrelizumab	23	40.4 (mean)	11 (mean) 5.67 (SD)	0 (0%)	NR	3.1 (mean) 1.5-6.5 (NR)
Vollmer (2021)	USA	Ocrelizumab	245	44.4 (mean)	9.6 (mean)	NR	NR	NR
Vollmer (2019)	USA	Ocrelizumab	357	45.1 (mean)	9.8 (mean)	NR	NR	NR

Abbreviations: ARR, annualized relapse rate; EDSS, expanded disability status scale; IQR, interquartile range; MS, multiple sclerosis; NA, not applicable; NR, not reported; SD, standard deviation

[a]Some studies include patients with secondary progressive MS, but ≥80% of the total study population were RRMS and/or PPMS

Table S3. Ocrelizumab discontinuation data

Author (year)	Country	Intervention	Line of intervention, n (%)	Switched from	Treatment period	Sample size	Patients who discontinued, n (%)	Reasons for discontinuation, n (%)	Time to discontinuation
Relapsing remitting MS (RRMS)									
Bewick (2020)	England	Ocrelizumab	First (42.8%) and switch	NR	NR	28	1 (3.5%)	Adverse events, 1 (3.5%)	NR
Bossart (2022)	Switzerland	Fingolimod	NR	NR	6 months	139	1 (0.7%)	NR	NR
		Dimethyl fumarate	NR	NR	6 months	104	6 (5.8%)	NR	NR
		Ocrelizumab	NR	NR	6 months	98	10 (10.2%)	NR	NR
		Natalizumab	NR	NR	6 months	44	3 (6.8%)	NR	NR
		Teriflunomide	NR	NR	6 months	31	1 (3.2%)	NR	NR
Evertsson (2020)	Sweden, USA	Ocrelizumab	First, 7 (4.34%) and switch	NR	NR	161	25 (15.5%)	Adverse events, 15 (9.3%) Lack of effect, 5 (3.1%) Lost to follow up, 3 (1.9%) Other reasons, 2 (1.2%)	NR
		Rituximab	First, 80 (25.7) and switch	NR	NR	311	NR (10%)	Adverse events, 8 (2.6%) Lack of effect, 5 (1.6%) Lost to follow up, 2 (0.6%) Other reasons, 5 (1.6%) Stable disease, 10 (3.2%) Pregnancy confirmed, 1 (0.3%)	NR

Author (year)	Country	Intervention	Line of intervention, n (%)	Switched from	Treatment period	Sample size	Patients who discontinued, n (%)	Reasons for discontinuation, n (%)	Time to discontinuation
Frahm (2022)	Germany	Ocrelizumab	Switch	Fingolimod	NR	178	3 (1.7%)	Switch, 2 (1.1%) Stop, 1 (0.6%)	NR
Garcia-Canibano (2021)	Qatar	Ocrelizumab	First line, NR (38%) and switch, NR (62%)	Various	19 months (median)	57	1 (1.8%)	Unplanned pregnancy, 1 (1.8%)	NR
Ozakbas (2021)	NR	Ocrelizumab	NR	NR	6 months	87	0 (0%)	NA	NA
Pontieri (2022)	Denmark	Ocrelizumab	First line, 118 (12.5%) Switch, 828 (87.5%)	Various	1.2 years (mean)	946	51 (4.6%)	Adverse events, 23 (2.4%) Pregnancy plans, 10 (1.1%) Progression, 6 (0.6%) Lack of compliance, 6 (0.6%) Death, 3 (0.3%) Unspecified reasons, 3 (0.3%)	0.6 years (median)
Rojas (2021)	Argentina, Chile, Mexico	Ocrelizumab	First-line, 7 and switch, 45	Various	>12 months	52	1 (1.9%)	Other, 1 (1.9%)	NR
Smoot (2019)	USA	Ocrelizumab	Switch	Natalizumab	12 months	21	0 (0%)	NA	NA
Weber (2022)	Germany	Ocrelizumab	First-line, 294 (17.3%)	Various	1.03 years (mean)	1702	80 (4.7%)	Adverse events, 13 (0.8%) Patient wish, 37 (2.2%) Insufficient efficacy, 12 (0.7%)	NR

Author (year)	Country	Intervention	Line of intervention, n (%)	Switched from	Treatment period	Sample size	Patients who discontinued, n (%)	Reasons for discontinuation, n (%)	Time to discontinuation
								Pregnancy wish, 6 (0.4%) Pregnancy, 4 (0.2%) Other, 8 (0.5%)	
Zanghi (2021)	Italy	Ocrelizumab	Switch	Natalizumab	18 months (median)	64	0 (0%)*	NA	NA
		Rituximab	Switch	Natalizumab	17 months (median)	36	0 (0%)*	NA	NA
		Cladribine	Switch	Natalizumab	16 months (median)	20	0 (0%)*	NA	NA
Zivadinov (2022)	USA	Ocrelizumab	Switch	Various	24 months	27	4 (14.8%)	Adverse events, 1 (3.7%) Patient decisions in relation to COVID-19, 3 (11.1%)	NR
Primary progressive MS (PPMS)									
Braune (2021)	Germany	Ocrelizumab	NR	NR	12 months	77	1 (1.3%)	NR	NR
Lopez-Ruiz (2020)	Spain	Ocrelizumab	First-line, 12 (66.7%) and Switch, 6 (33.3%)	Various	13.8 months (mean)	18	0 (0%)	NA	NA
Ozakbas (2021)	NR	Ocrelizumab	NR	NR	6 months	42	0 (0%)	NA	NA
Rojas (2021)	Argentina, Chile, Mexico	Ocrelizumab	First-line, 12 (NR) and switch	Various	>12 months	29	2 (6.7%)	Poor tolerability, 1 (3.4%) Disease activity, 1 (3.4%)	NR
Weber (2022)	Germany	Ocrelizumab	First-line, 268 (67.3%)	Various	1.06 years (mean)	398	19 (4.8%)	Adverse events, 4 (1.0%) Patient wish, 9 (2.3%)	NR

Author (year)	Country	Intervention	Line of intervention, n (%)	Switched from	Treatment period	Sample size	Patients who discontinued, n (%)	Reasons for discontinuation, n (%)	Time to discontinuation
								Insufficient efficacy, 3 (0.8%) Other, 3 (0.8%)	
Relapsing remitting MS and primary progressive MS combined population[†]									
Baghestani (2020)	UAE	Ocrelizumab	First (23%) and switch	Various	9.6 months (mean)	27	2 (7.4%)	Lost to follow up, 2 (7.7%)	
Butzkueven (2021)	Australia, Turkey, Kuwait, Belgium	Ocrelizumab	First, NR (13%) and switch	Various	NR	800	26 (3.3%)	NR	1.8 years (median)
Butzkueven (2019)	Europe and Australia	Ocrelizumab	First and switch, NR	Various	12 months	1216	1.6%	NR	NR
					24 months	1216	7.5%	NR	NR
Braune (2020)	Germany	Ocrelizumab	First and switch, NR	Various	≥3 months	439	0 (0%)	NA	NA
Cellerino (2021)	Italy	Ocrelizumab	NR	NR	24 months	153	6 (3.9%)	Adverse effects, 6 (3.9)	NR
Coban (2021)	USA	Ocrelizumab	First line, 39 (47%) Switch, 43 (53%)	Various	NR	82	4 (4.8%)	NR	NR
Ellwardt (2020)	Germany	Ocrelizumab	First, NR (24%) and switch, NR (76%)	Various	NR	210	1 (0.5%) (Temporarily discontinued)	Adverse events, 1 (0.5%)	5 months
Fernandez-Diaz (2021)	Spain	Ocrelizumab	First-line, 83 (36.4%) and switch, 145 (63.6%)	Various	12 months	228	5 (2.2%)	Death Pregnancy Patient's choice Ineffectiveness	NR
Finder (2020)	USA	Ocrelizumab	First-line, 69 (38.8%)	NR	NR	178	0 (0%)	NR	NR
		Fingolimod	NR	NR	NR	NR	8 (NR)	NR	NR

Author (year)	Country	Intervention	Line of intervention, n (%)	Switched from	Treatment period	Sample size	Patients who discontinued, n (%)	Reasons for discontinuation, n (%)	Time to discontinuation
		Dimethyl fumarate	NR	NR	NR	NR	17 (NR)	NR	NR
		Teriflunomide	NR	NR	NR	NR	10 (NR)	NR	NR
Luxenberg (2021)	USA	Ocrelizumab	NR	NR	NR	59	14 (23.7%)	Adverse events, 5 (8.5%) MS progression, 5 (8.5%) Receiving autologous stem cell transplant, 1 (1.7%) Unfavorable risk/benefit ratio, 2 (3.4%) Worsening psoriasis, 1 (1.7%)	NR
Magyari (2020)	Denmark	Ocrelizumab	First line, 131 (41 of which were PPMS) and switch	NR	NR	851	18 (2.1%)	Adverse effects, 9 (1.1%) Disease breakthrough, 2 (0.2%)	NR
Pontieri (2022)	Denmark	Ocrelizumab	First line, 166 Switch, 841	Various	NR	1104	51 (4.6%)	Adverse effects, 23 Pregnancy plans, 10 Progression, 6 Lack of compliance, 6 Death, 3 Unspecified reasons, 3	0.6 years (median)

Author (year)	Country	Intervention	Line of intervention, n (%)	Switched from	Treatment period	Sample size	Patients who discontinued, n (%)	Reasons for discontinuation, n (%)	Time to discontinuation
Sempere (2020)	Spain	Ocrelizumab	First line, 29 (41%) Switch, 42 (59%)	NR	13.6 months (mean)	70	2 (2.9%)	Pregnancy, 1 Lack of efficacy, 1	NR
Smoot (2022)	USA	Ocrelizumab	NR	NR	34.3 months (median)	509	129 (25.3%)	Adverse events, 63 (12.4%)	20.5 months (median)
Tsantes (2020)	Italy	Ocrelizumab	Switch	Natalizumab	15 months	23	0 (0%)	NA	NA
Vollmer (2021)	USA	Ocrelizumab	NR	NR	Up to 24 months	245	51 (20.8%)	Adverse events, 2 (0.8%) Insurance issues, 17 (6.9%) Lost to follow up, 22 (9.0%) Other reasons (e.g., family planning, concern for cancer, preference for no treatment), 10 (4.1%)	NR
Vollmer (2019)	USA	Ocrelizumab	NR	NR	Up to 12 months	357	19 (5.3%)	NR	NR

Abbreviations: MS, multiple sclerosis; NA, not applicable; NR, not reported

*number of patients who discontinued for safety concerns

[†]Some studies include patients with secondary progressive MS, but ≥80% of the total study population were RRMS and/or PPMS