## Supplementary data

## Supplementary Method 1: Search strategy

MEDLINE search strategy:

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to March 22, 2022>

Search Strategy:

1 exp Multiple Sclerosis, Relapsing-Remitting/ 7456

2 exp Multiple Sclerosis, Chronic Progressive/ 2392

3 ((("multiple sclerosis" or MS) adj2 (relapsing$ or remitting$ or primary$ or progressive$)) or RRMS or PPMS).ti,ab. 14289

4 or/1-3 16881

5 (ocrelizumab or Ocrevus$).ti,ab. 565

6 Epidemiologic studies/ 9039

7 exp case control studies/ 1298467

8 exp cohort studies/ 2315892

9 Case control.tw. 141660

10 (cohort adj (study or studies)).tw. 266018

11 Cohort analy$.tw. 10082

12 (Follow up adj (study or studies)).tw. 53184

13 (observational adj (study or studies)).tw. 136749

14 Longitudinal.tw. 287636

15 Retrospective.tw. 649234

16 Cross sectional.tw. 439907

17 Cross-sectional studies/ 416516

18 or/6-17 3478538

19 4 and 5 and 18 59

Embase search strategy:

Searched 23/03/22 via OvidSP interface.

Database: Embase <1974 to 2022 March 22>

Search Strategy:

1 exp Multiple Sclerosis, Relapsing-Remitting/ 143903

2 exp Multiple Sclerosis, Chronic Progressive/ 143903

3 ((("multiple sclerosis" or MS) adj2 (relapsing$ or remitting$ or primary$ or progressive$)) or RRMS or PPMS).ti,ab. 30632

4 or/1-3 146617

5 (ocrelizumab or Ocrevus$).ti,ab. 1501

6 Clinical study/ 157579

7 Case control study/ 185675

8 Family study/ 25397

9 Longitudinal study/ 169653

10 Retrospective study/ 1218722

11 Prospective study/ 753983

12 Randomized controlled trials/ 222820

13 11 not 12 745255

14 Cohort analysis/820627

15 (Cohort adj (study or studies)).mp. 392500

16 (Case control adj (study or studies)).ti,ab. 152390

17 (follow up adj (study or studies)).ti,ab. 68742

18 (observational adj (study or studies)).ti,ab. 212417

19 (epidemiologic$ adj (study or studies)).ti,ab. 115039

20 (cross sectional adj (study or studies)).ti,ab. 281701

21 or/6-10,13-20 3358910

22 (conference or "conference paper" or "conference proceeding" or "conference proceeding article" or "conference proceeding conference paper" or "conference proceeding editorial" or "conference proceeding note" or "conference proceeding review" or "journal conference abstract" or "journal conference paper" or "journal conference review").pt. 5127456

23 21 not 22 2470461

24 4 and 5 and 21 432

25 4 and 5 and 23 129

## Supplementary Table 1. PICOS elements, inclusion, and exclusion criteria

| Element | Inclusion Criteria | Exclusion criteria |
|---|---|---|
| **P**opulation | • 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 |
| **I**ntervention | • Ocrelizumab | • NA |
| **C**omparator(s) | • Any/none | • NA |
| **O**utcome(s) | • Clinical effectiveness in RRMS or PPMS patients, including:<br>  ○ No evidence of progression and no active disease (NEPAD) or no evidence of disease activity (NEDA)<br>  ○ Relapse activity/rate<br>  ○ Time to onset of confirmed disability progression (CDP)<br>  ○ Change in cognitive function [e.g., Symbol Digit Modalities Test (SDMT)]<br>  ○ Change in Expanded Disability Status Scale (EDSS) score<br>• Health-related quality of life (HRQoL) | • Outcomes not listed in this section |
| **S**tudy type(s) | • Observational/real-world evidence studies (prospective/retrospective cohort, cross sectional, case control, case series) of sufficient sample size (e.g., ≥ 10 patients)<br>• Any country<br>• English language studies | • Studies not reporting real-world evidence (e.g., RCTs, cost-effectiveness models)<br>• Non-English language studies |

## Supplementary Table 2. 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)** | | | | | | | | |
| Bigaut (2022)[a] [1] | Full text | France | 102 | RRMS | 102 | × | ✓ | 1 year |
| Bossart (2022) [2] | Full text | Switzerland | 668 | RRMS | 416 | NR | NR | 6 months |
| Buttmann (2021) [3] | Abstract | Germany | 1510 | RMS | NR | ✓ | ✓ | 6-12 months |
| Cellerino (2021)[a] [4] | Abstract | Italy | 33 | RRMS | 17 | NR | NR | 2 years |
| Fan (2021) [5] | Abstract | USA | 86 | RRMS | 86 | NR | NR | 2 years |
| Frahm (2022)[a] [6] | Full text | Germany | 2536 | RRMS | 2536 | × | ✓ | 6-12 months |
| Garcia-Canibano (2021)[a] [7] | Full text | Qatar | 60 | RRMS | 57 | ✓ | ✓ | 1 year |
| Lanzillo (2021) [8] | Abstract | Italy | 383 | RRMS | 89 | NR | NR | 1 year |
| Lopez Ruiz (2021)[a] [9] | Abstract | Spain | 52 | RRMS | 52 | ✓ | ✓ | 1 year |
| Mancinelli (2020) [10] | Full text | Italy | 42 | RRMS | 42 | × | ✓ | 3-6 months |
| Neo (2020)[a] [11] | Abstract | England | 170 | RRMS | 170 | ✓ | ✓ | 4-6 months |
| Pasanisi (2020) [12] | Abstract | Italy | 42 | RRMS | 42 | × | ✓ | 3-4 months |
| Rolfes (2021)[a] [13] | Full text | Germany | 318 | RRMS | 318 | ✓ | ✓ | 3 months following 3rd dose |
| Smoot (2021)[a] [14] | Abstract | NR | 43 | RRMS | 43 | × | ✓ | 1-2 years |
| Treffts (2021) [15] | Abstract | Germany and Denmark | 223 | RRMS | 223 | × | ✓ | 6 months |
| Van Kesteren (2021) [16] | Abstract | Germany, Norway, Denmark | 254 | RRMS | 254 | × | ✓ | 6 months |

| 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 | |
| Zanghi (2021)[a] [17] | Full text | Italy | 120 | RRMS | 120 | × | ✓ | 6-18 months |
| Zhong (2021)[a] [18] | Full text | Global | 1096 | RRMS | 1096 | × | ✓ | <1 year |
| **Primary progressive MS (PPMS)** | | | | | | | | |
| Alcala (2022) [19] | Full text | Spain | 95 | PPMS | 95 | ✓ | ✓ | 18 months (mean follow-up) |
| Braune (2021) [20] | Abstract | Germany | 460 | PPMS | 460 | NR | NR | 1 year |
| Daniels (2020) [21] | Full text | Netherlands | 21 | PPMS | 21 | NR | NR | NR |
| Impellizzeri (2019) [22] | Abstract | Italy | 54 | PPMS | 54 | NR | NR | 1 year |
| Lopez Ruiz (2020) [23] | Abstract | Spain | 18 | PPMS | 18 | ✓ | ✓ | 13.8 months (mean follow-up) |
| Miscioscia (2021) [24] | Abstract | NR | 27 | PPMS | 27 | NR | NR | 2 years |
| Novi (2018) [25] | Abstract | NR | 34 | PPMS | 34 | ✓ | ✓ | 4.5 months (median follow-up) |
| Pereira Coutinho (2021)[a] [26] | Abstract | NR | 51 | PPMS | 51 | NR | NR | 19 months (median follow-up) |
| **Relapsing remitting and primary progressive MS (stratified)** | | | | | | | | |
| Braune (2020) [27] | Abstract | Germany | 439 | RRMS | 352 | ✓ | ✓ | >3 months |
| | | | | PPMS | 52 | ✓ | ✓ | |
| | | | | SPMS | 35 | ✓ | ✓ | |
| Butzkueven (2019) [28] | Abstract | Various countries in North and South America, Europe, Middle East & Oceania | 1216 | RRMS | 882 | ✓ | ✓ | >6 months |
| | | | | PPMS | 174 | ✓ | ✓ | |
| | | | | SPMS | 160 | ✓ | ✓ | |
| Coban (2021)[a] [29] | Full text | US | 82 | RRMS | 59 | ✓ | ✓ | NR |
| | | | | SPMS | 9 | ✓ | ✓ | |
| | | | | PPMS | 14 | ✓ | ✓ | |
| Fernandez-Diaz (2021)[a] [30] | Full text | Italy | 228 | RRMS | 144 | ✓ | ✓ | 10-19 months (median follow-up) |
| | | | | SPMS | 25 | ✓ | ✓ | |

| 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 | |
| | | | | PPMS | 59 | ✓ | ✓ | |
| Guerra (2021) [31] | Abstract | Italy | 133 | RRMS | 76 | NR | NR | 1.80-2.09 years (median follow-up) |
| | | | | PPMS | 35 | NR | NR | |
| Ozakbas (2021) [32] | Abstract | NR | 304 | RRMS | 87 | NR | NR | 6 months |
| | | | | PPMS | 42 | NR | NR | |
| Pontieri (2022)[a] [33] | Full text | Denmark | 1104 | RRMS | 946 | ✓ | ✓ | 6-18 months |
| | | | | PPMS | 61 | ✓ | ✓ | |
| | | | | SPMS | 97 | ✓ | ✓ | |
| Prockl (2020) [34] | Full text | Germany | 128 | RRMS | 86 | ✓ | ✓ | NR |
| | | | | PPMS | 42 | ✓ | ✓ | |
| Rojas (2021)[a] [35] | Full text | Argentina, Chile, Mexico | 81 | RRMS | 52 | ✓ | ✓ | >1 year |
| | | | | PPMS | 29 | ✓ | ✓ | |
| Signoriello (2022) [36] | Full text | Italy | 165 | RRMS | 114 | × | ✓ | 6 months |
| | | | | PMS | 51 | × | ✓ | |
| Signoriello (2020) [37] | Full text | Italy | 108 | RRMS | 34 | ✓ | ✓ | 1 year |
| | | | | PPMS | 19 | ✓ | ✓ | |
| | | | | SPMS | 55 | ✓ | ✓ | |
| **Relapsing remitting and primary progressive MS (not stratified)** | | | | | | | | |
| Butzkueven (2021) [38] | Full text | Argentina, Australia, Belgium, Canada, Spain, Turkey, Kuwait, and Mexico | 800 | RRMS | NR | ✓ | ✓ | 6 months |
| | | | | PPMS | NR | ✓ | ✓ | |
| | | | | SPMS | NR | ✓ | ✓ | |
| Cellerino (2021) [39] | Full text | Italy | 153 | RRMS | 93 | NR | NR | 2 years |
| | | | | PPMS | 43 | NR | NR | |
| | | | | SPMS | 17 | NR | NR | |
| Ellwardt (2020) [40] | Full text | Germany | 210 | RRMS/aSPMS | 155 | ✓ | ✓ | 200 days (median follow-up) |
| | | | | PPMS | 55 | ✓ | ✓ | |
| Geils (2020) [41] | Abstract | US | 291 | RRMS | 183 | NR | NR | NR |
| | | | | PMS[b] | 108 | NR | NR | |
| Magyari (2020) [42] | | Denmark | 851 | RRMS | 735 | ✓ | ✓ | 6-12 months |

| 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 | |
| | Abstract | | | SPMS | 61 | ✓ | ✓ | |
| | | | | PPMS | 55 | ✓ | ✓ | |
| Moss (2019) [43] | Abstract | NR | 272 | RRMS | 208 | NR | NR | 6 months |
| | | | | PPMS | 64 | NR | NR | |
| Sempere (2020)[a] [44] | Full text | Spain | 70 | RMS | 49 | ✓ | ✓ | 2 years |
| | | | | PPMS | 21 | ✓ | ✓ | |
| Smoot (2021) [45] | Full text | US | 355 | RRMS | 278 | ✓ | ✓ | 2 years |
| | | | | SPMS | 47 | ✓ | ✓ | |
| | | | | PPMS | 30 | ✓ | ✓ | |
| Smoot (2018) [46] | Abstract | US | 223 | RMS | 164 | ✓ | ✓ | NR |
| | | | | SPMS | 38 | ✓ | ✓ | |
| | | | | PPMS | 21 | ✓ | ✓ | |
| Toorop (2021) [47] | Full text | The Netherlands | 117 | RRMS | 92 | NR | NR | 1.7 years (mean follow-up) |
| | | | | SPMS | 4 | NR | NR | |
| | | | | PPMS | 21 | NR | NR | |
| Tsantes (2020) [48] | Abstract | Italy | 23 | RRMS | 17 | × | ✓ | 6 months |
| | | | | Progressive active MS | 6 | × | ✓ | |
| Van Lierop (2021) [49] | Full text | Netherlands | 165 | RRMS | 127 | ✓ | ✓ | 45 weeks (median follow-up) |
| | | | | SPMS | 8 | ✓ | ✓ | |
| | | | | PPMS | 31 | ✓ | ✓ | |
| Vollmer (2021) [50] | Abstract | USA | 245 | RRMS | 200 | NR | NR | NR |
| | | | | SPMS | 37 | NR | NR | |
| | | | | PPMS | 8 | NR | NR | |
| Vollmer (2019) [51] | Abstract | USA | 357 | RRMS | 267 | NR | NR | 1 year |
| | | | | SPMS | 59 | NR | NR | |
| | | | | PPMS | 31 | NR | NR | |
| Yousuf (2020) [52] | Abstract | Qatar | 65 | RRMS | 52 | ✓ | ✓ | 2 years |
| | | | | PPMS | 5 | ✓ | ✓ | |

| 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 | 3 | ✓ | ✓ | |

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

[a]Studies presented in Figure 2 and/or Figure 3

[b]PPMS and progressive RRMS

## Supplementary Table 3. Overview of baseline characteristics

| Author (year) | Country | Intervention | Sample size | Age | Disease duration (years) | No previous therapy, n (%) | ARR | EDSS |
|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | |
| Bigaut (2022) [1] | France | Ocrelizumab | 48 | 40.6 (mean)<br>10.3 (SD) | 13.5 (mean)<br>6.8 (SD) | 0 | 0.15 (mean)<br>0.36 (SD) | 2.4 (mean)<br>1.7 (SD) |
| | | Fingolimod | 54 | 39.5 (mean)<br>9.3 (SD) | 11.5 (mean)<br>6.7 (SD) | 0 | 0.29 (mean)<br>0.62 (SD) | 2.8 (mean)<br>1.7 (SD) |
| Bossart (2022) [2] | Switzerland | Fingolimod | 139 | 46.1 (mean)<br>9.9 (SD) | 9.7 (mean)<br>6.4 (SD) | 7 (5%) | NR | NR |
| | | Dimethyl fumarate | 104 | 44 (mean)<br>11.5 (SD) | 8.6 (mean)<br>8.0 (SD) | 13 (12.5%) | NR | NR |
| | | Ocrelizumab | 98 | 43.9 (mean)<br>11.9 (SD) | 9.8 (mean)<br>6.7 (SD) | 23 (24%) | NR | NR |
| | | Natalizumab | 44 | 42.9 (mean)<br>11.9 (SD) | 11.8 (mean)<br>7.0 (SD) | 6 (14%) | NR | NR |
| | | Teriflunomide | 31 | 50.9 (mean)<br>9.8 (SD) | 9.7 (mean)<br>8.2 (SD) | 4 (13%) | NR | NR |
| Buttmann (2021) [3] | Germany | Ocrelizumab | 1510 | NR | NR | NR | NR | NR |
| Cellerino (2021) [4] | Italy | Ocrelizumab | 17 | NR | NR | NR | NR | NR |
| Cellerino (2021) [39] | Italy | Ocrelizumab | 93 | 36.9 (mean)<br>10.2 (SD) | 9.3 (mean)<br>9.2(SD) | NR | 0.8 (mean)<br>0.7 (SD) | 2 (median)<br>2-3.5 (IQR) |
| Coban (2021) [29] | US | Ocrelizumab | 59 | 38 (mean)<br>11 (SD) | 7.6 (mean)<br>9.8 (SD) | 25 (42%) | 1.4 (mean)<br>0.9 (SD) | 2.2 (mean)<br>1 (SD) |
| Fan (2021) [5] | USA | Ocrelizumab | 86 | NR | NR | NR | NR | NA |
| Fernandez-Diaz (2021) [30] | Spain | Ocrelizumab | 144 | 39.5 (mean) | 7.28 (mean)<br>6.63 (SD) | 36 (25%) | 1.12 (mean)<br>0.77 (SD) | 2.8 (mean)<br>1.6 (SD) |

| Author (year) | Country | Intervention | Sample size | Age | Disease duration (years) | No previous therapy, n (%) | ARR | EDSS |
|---|---|---|---|---|---|---|---|---|
| Frahm (2022) [6] | Germany | Ocrelizumab | 178 | 41.8 (mean)<br>10.3 (SD) | NR | 0 | 0.32 (NR) | 3.5 (median) |
| Garcia-Canibano (2021) [7] | Qatar | Ocrelizumab | 57 | 34.9 (mean)<br>10.4 (SD) | 7 (mean)<br>6.63 (SD) | 24 (38%) | NR | 2.1 (mean)<br>2.4 (SD) |
| Guerra (2021) [31] | Italy | Ocrelizumab | 76 | 43.5 (mean)<br>20.5-60.6 (SD) | 12.9 (mean)<br>0.5-41.2 (SD) | NR | NR | 4 (median)<br>1-7.5 (IQR) |
| Lanzillo (2021) [8] | Italy | Ocrelizumab | 89 | NR | NR | NR | NR | NR |
| Lopez Ruiz (2021) [9] | Spain | Ocrelizumab | 52 | 39.5 (mean)<br>8.7 (SD) | 11.1 (mean)<br>1-27.3 (range) | 5 | 1 (median) | 3.5 (median)<br>1.5-6.5 (IQR) |
| Mancinelli (2020) [10] | Italy | Ocrelizumab | 42 | NR | NR | 0 | 0 (median) | 3 (median)<br>0-8 (range) |
| Neo (2020) [11] | England | Ocrelizumab | 170 | 45.5 (mean) | 13.1 (mean) | 25 (14.7%) | NR | 4.3 (mean) |
| Ozakbas (2021) [32] | NR | Ocrelizumab | 87 | NR | 17.7 (mean) | NR | NR | NR |
| Pasanisi (2020) [12] | Italy | Ocrelizumab | 42 | 42 (mean)<br>9 (SD) | 11 (mean)<br>6 (SD) | 0 | NR | 4 (mean) |
| Pontieri (2022) [33] | Denmark | Ocrelizumab | 946 | 41.4 (mean)<br>10.2 (SD) | 10.8 (mean)<br>8.2 (SD) | 118 (12.5%) | 0.6 (mean)<br>0.8 (SD) | 2.9 (mean)<br>1.7 (SD) |
| Rolfes (2021) [13] | Germany | Ocrelizumab (standard interval dosing) | 202 | 43 (median)<br>33-51.8 (IQR) | 8.8 (median)<br>3.8-15.9 (IQR) | 38 (20.1%) | 1 (median)<br>0-1 (IQR) | 3.3 (median)<br>2-6 (IQR) |
| | | Ocrelizumab (extended interval dosing) | 116 | 40 (median)<br>32-49 (IQR) | 8.6 (median)<br>3.4-15.2 (IQR) | 24 (21.3%) | 1 (median)<br>0-1 (IQR) | 3.5 (median)<br>2-6 (IQR) |
| Sempere (2020) [44] | Spain | Ocrelizumab | 49 | 39.2 (mean)<br>10.9 (SD) | 7.7 (mean)<br>6.7 (SD) | 10 (20%) | 1.3 (mean)<br>0.65 (SD) | 2.5 (median)<br>2-3 (IQR) |

| Author (year) | Country | Intervention | Sample size | Age | Disease duration (years) | No previous therapy, n (%) | ARR | EDSS |
|---|---|---|---|---|---|---|---|---|
| Smoot (2021) [45] | US | Ocrelizumab | 278 | NR | 12 (median)<br>6.5-18.4 (IQR) | 59 (21.5%) | 0.34 (mean)<br>0.42 (SD) | 3 (median)<br>2-4 (IQR) |
| Smoot (2021) [14] | NR | Ocrelizumab | 43 | NR | NR | 0 | NR | 3.5 (median)<br>2.25 (IQR) |
| Treffts (2021) [15] | Germany and Denmark | Ocrelizumab | 196 | NR | NR | 0 | NR | NR |
| | | Cladribine | 27 | NR | NR | 0 | NR | NR |
| Van Kesteren (2021) [16] | Germany, Norway, Denmark | Ocrelizumab | 196 | NR | NR | 0 | NR | NR |
| | | Cladribine | 58 | NR | NR | 0 | NR | NR |
| Zanghi (2021) [17] | Italy | Ocrelizumab | 64 | NR | NR | 0 | NR | 3 (median)<br>2-4.5 (IQR) |
| | | Rituximab | 36 | NR | NR | 0 | NR | 4 (median)<br>2-4.5 (IQR) |
| | | Cladribine | 20 | NR | NR | 0 | NR | 2 (median)<br>1-3 (IQR) |
| Zhong (2021) [18] | Global | Ocrelizumab | 1,096 | 42.7 (mean)<br>10.9 (SD) | 11.4 (mean)<br>7.5 (SD) | 0 | NR | 3 (median)<br>1.5-4.5 (IQR) |
| **Primary progressive MS** | | | | | | | | |
| Alcala (2022) [19] | Spain | Rituximab | 49 | 51.1 (mean)<br>9.8 (SD) | 8.4 (mean)<br>6.3 (SD) | 19 (39%) | NR | 5.4 (mean)<br>1.6 (SD) |
| | | Ocrelizumab | 46 | 48.8 (mean)<br>9 (SD) | 5.3 (mean)<br>5.3 (SD) | 40 (87%) | NR | 4.7 (mean)<br>1.3 (SD) |
| Braune (2021) [20] | Germany | Any | 460 | 62.29 (mean)<br>11.35 (SD) | 18.7 (mean)<br>11.0 (SD) | NR | NR | NR |
| | | Ocrelizumab | 82 | 51.5 (mean)<br>10.03 (SD) | 8.7 (mean)<br>7.8 (SD) | NR | NR | NR |

| Author (year) | Country | Intervention | Sample size | Age | Disease duration (years) | No previous therapy, n (%) | ARR | EDSS |
|---|---|---|---|---|---|---|---|---|
| Cellerino (2021) [39] | Italy | Ocrelizumab | 43 | 49.2 (mean)<br>8.6 (SD) | 8.4 (mean)<br>6.5 (SD) | NR | NR | 5.5 (median)<br>3.5-6.5 (IQR) |
| Coban (2021) [29] | US | Ocrelizumab | 14 | 46 (mean)<br>10 (SD) | 3.5 (mean)<br>3.7 (SD) | 11 (79%) | NR | 4.6 (mean)<br>1.5 (SD) |
| Daniels (2020) [21] | Netherlands | Ocrelizumab | 21 | 52.09 (mean)<br>6.42 (SD) | NA | NR | NR | 5.33 (mean)<br>1.13 (SD) |
| Fernandez-Diaz (2021) [30] | Spain | Ocrelizumab | 59 | 48.4 (mean)<br>9.3 (SD) | 4.18 (mean)<br>4.94 (SD) | 46 (78%) | NR | 4.75 (mean)<br>1.43 (SD) |
| Guerra (2021) [31] | Italy | Ocrelizumab | 35 | 51.6 (mean)<br>33.6-68.6 (SD) | 8 (mean)<br>0.9-31.5 (SD) | NR | NR | 5.5 (median)<br>4-8 (IQR) |
| Impellizzeri (2019) [22] | NA | Ocrelizumab | 54 | 46 (mean)<br>23-66 (range) | 7 (mean)<br>1-19 (range) | NR | NR | 4.5 (median)<br>3-8 (range) |
| Lopez Ruiz (2020) [23] | Spain | Ocrelizumab | 18 | 47 (NR)<br>37-57 (NR) | 5.4 (mean)<br>0.5-12.3 (NR) | 12 (67%) | NR | 5.7 (mean) |
| Miscioscia (2021) [24] | NR | Ocrelizumab | 27 | 51.6 (mean)<br>6.4 (SD) | NR | NR | NR | NR |
| Novi (2018) [25] | NR | Ocrelizumab | 34 | 52 (mean)<br>36-66 (range) | 12.4 (mean) | 10 (29%) | NR | 6 (median)<br>2-7.5 (range) |
| Ozakbas (2021) [32] | NR | Ocrelizumab | 42 | NR | 17.7 (mean) | NR | NR | NR |
| Pereira Coutinho (2021) [26] | NR | Ocrelizumab | 51 | NR | 8 (median)<br>1-24 (range) | NR | NR | NR |
| Pontieri (2022) [33] | Denmark | Ocrelizumab | 61 | 44.5 (mean)<br>6.9 (SD) | 6.6 (mean)<br>3.7 (SD) | 48 (79%) | 0.1 (mean)<br>0.2 (SD) | 4 (mean)<br>1.6 (SD) |
| Sempere (2020) [44] | Spain | Ocrelizumab | 21 | 47.1 (mean)<br>10.5 (SD) | 2.8 (mean)<br>4.1 (SD) | 19 (90%) | NR | 3 (median)<br>3-4.8 (IQR) |

| Author (year) | Country | Intervention | Sample size | Age | Disease duration (years) | No previous therapy, n (%) | ARR | EDSS |
|---|---|---|---|---|---|---|---|---|
| Smoot (2021) [45] | US | Ocrelizumab | 30 | NR | 12.7 (mean)<br>7.7-17.2 (IQR) | 17 (59%) | 0 (mean) | 6.5 (median)<br>6-7 (IQR) |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | |
| Braune (2020) [27] | Germany | Ocrelizumab | 439 | NR | NR | NR | NR | NR |
| Butzkueven (2021) [38] | Australia, Turkey, Kuwait, Belgium | Ocrelizumab | 800 | 42.7 (median)<br>35.2-50.4 (IQR) | 12.4 (mean)<br>8.3 (SD) | 104 (13%) | NR | NR |
| Butzkueven (2019) [28] | Europe & Australia | Ocrelizumab | 1216 | NR | NR | 204 (16.8%) | NR | NR |
| Cellerino (2021) [39] | Italy | Ocrelizumab | 153 | 41.9 (mean)<br>11.4 (SD) | 16.05 (mean)<br>9.9 (SD) | NR | 0.5 (mean)<br>0.7 (SD) | 3.5 (median)<br>2-5.5 (IQR) |
| Coban (2021) [29] | US | Ocrelizumab | 82 | 40 (mean) | 8.0 (mean) | 39 (47%) | 1.4 (mean)<br>0.9 (SD) | 3.1 (mean)<br>1.8 (SD) |
| Ellwardt (2020) [40] | Germany | Ocrelizumab | 210 | 42.1 (mean) | 7.2 (mean) | 50 (24%) | NR | 3.9 (mean) |
| Fernandez-Diaz (2021) [30] | Spain | Ocrelizumab | 228 | 42.7 (mean)<br>11.2 (SD) | 6.98 (mean)<br>6.66 (SD) | 83 (36.4%) | 1.11 (mean)<br>0.81 (SD) | 3.58 (mean)<br>1.83 (SD) |
| Geils (2020) [41] | US | Ocrelizumab | 291 | 18-73 (range) | NR | NR | NR | 3 (median)<br>0-7 (range) |
| Magyari (2020) [42] | Denmark | Ocrelizumab | 851 | NR | NR | 131 (15.4%) | NR | NR |
| Moss (2019) [43] | NR | Ocrelizumab | 272 | 47 (median) | 13 (NR) | NR | NR | NR |
| Prockl (2020) [34] | Germany | Ocrelizumab | 128 | 41 (mean)<br>18-76 (range) | 6.25 (median)<br>3.1-14.3 (IQR) | 5 (3.9%) | NR | 3.5 (median)<br>2-5 (IQR) |
| Rojas (2021) [35] | Argentina, Chile, Mexico | Ocrelizumab | 81 | 41.3 (mean)<br>12 (SD) | 8.4 (mean)<br>6.3 (SD) | 29 (24%) | 1.3 (mean)<br>0.6 (SD) | 3.1 (mean)<br>1.8 (SD) |

| Author (year) | Country | Intervention | Sample size | Age | Disease duration (years) | No previous therapy, n (%) | ARR | EDSS |
|---|---|---|---|---|---|---|---|---|
| Sempere (2020) [44] | Spain | Ocrelizumab | 70 | 41.6 (mean) | 6.53 (mean) | 29 (41%) | NR | NR |
| Signoriello (2020) [37] | Italy | Ocrelizumab | 108 | 44.5 (mean)<br>10.6 (SD) | 13.08 (mean)<br>8 (SD) | 23 (21.3%) | 0.55 (mean) | 5.06 (mean)<br>2.02 (SD) |
| Signoriello (2022) [36] | Italy | Ocrelizumab | 165 | 40.3 (mean)<br>10.3 (SD) | 13.4 (mean)<br>1.1-38 (range) | 0 | 0.47 (mean)<br>0.7 (SD) | 4 (median)<br>1-3 (IQR) |
| Smoot (2018) [46] | USA | Ocrelizumab | 223 | 51 (mean)<br>11.6 (SD) | NR | 53 (24.2%) | NR | NR |
| Smoot (2021) [45] | US | Ocrelizumab | 355 | 51.8 (mean)<br>12.5 (SD) | 13.1 (median)<br>7.6-19.3 (IQR) | 96 (27.4%) | NR | NR |
| Toorop (2021) [47] | The Netherlands | Ocrelizumab | 117 | 42.6 (mean)<br>10.7 (SD) | 10.3 (mean)<br>6.1 (SD) | NR | NR | 3.5 (median)<br>2.5-5 (IQR) |
| Tsantes (2020) [48] | Italy | Ocrelizumab | 23 | 40.4 (mean) | 11 (mean)<br>5.67 (SD) | 0 (0%) | NR | 3.1 (mean)<br>1.5-6.5 (NR) |
| Van Lierop (2021) [49] | Netherlands | Ocrelizumab | 165 | 42.8 (mean)<br>10.9 (SD) | 9.9 (median)<br>4.9-14.5 (IQR) | 39 (23.6%) | NR | 4 (median)<br>2.5-5 (IQR) |
| Vollmer (2021) [50] | USA | Ocrelizumab | 245 | 44.4 (mean) | 9.6 (mean) | NR | NR | NR |
| Vollmer (2019) [51] | USA | Ocrelizumab | 357 | 45.1 (mean) | 9.8 (mean) | NR | NR | NR |
| Yousuf (2021) [52] | Qatar | Ocrelizumab | 65 | 38.7 (mean) | 7.75 (mean)<br>6.72 (SD) | NR (32%) | 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

## Supplementary Table 4. Studies reporting number and/or percentage of patients experiencing clinical relapse

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | | | | | |
| Bigaut (2022) [1] | France | NA | Ocrelizumab | Switch | Natalizumab | 1 year | 48 | Number (and percentage) of patients with no relapses | 43 (90%) | NA | NR | NA |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 54 | Number (and percentage) of patients with no relapses | 37 (69%) | NA | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 1 year | 48 | Number (and percentage) of patients with 1 relapse | 4 (8%) | NA | NR | NA |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 54 | Number (and percentage) of patients with 1 relapse | 14 (26%) | NA | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 1 year | 48 | Number (and percentage) of | 1 (2%) | NA | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | patients with 2 relapses | | | | |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 54 | Number (and percentage) of patients with 2 relapses | 1 (2%) | NA | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 1 year | 48 | Number (and percentage) of patients with 3 relapses | 0 (0%) | NA | NR | NA |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 54 | Number (and percentage) of patients with 3 relapses | 2 (4%) | NA | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 1 year | 48 | Number (and percentage) of patients with relapses | 5 (10%) | NA | 0.04 | Ocrelizumab vs fingolimod |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 54 | Number (and percentage) of | 17 (32%) | NA | 0.04 | Ocrelizumab vs fingolimod |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | patients with relapses | | | | |
| Bossart (2022) [2] | Switzerland | NA | Fingolimod | NR | NA | 6 months | 139 | Number (and percentage) of patients with relapses | 16 (11.5%) | NA | NR | NA |
| | | | Dimethyl fumarate | NR | NA | 6 months | 104 | Number (and percentage) of patients with relapses | 12 (11.5%) | NA | NR | NA |
| | | | Ocrelizumab | NR | NA | 6 months | 98 | Number (and percentage) of patients with relapses | 11 (11%) | NA | NR | NA |
| | | | Natalizumab | NR | NA | 6 months | 44 | Number (and percentage) of patients with relapses | 6 (14%) | NA | NR | NA |
| | | | Teriflunomide | NR | NA | 6 months | 31 | Number (and percentage) of | 3 (10%) | NA | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | patients with relapses | | | | |
| Braune (2020) [27] | Germany | NA | Ocrelizumab | First line and switch | Fingolimod and natalizumab | >3 months (follow-up) | 439 | Number (and percentage) of patients who remained relapse free | 283 (88.7%) | 84.9-91.8 (95% CI) | NR | NA |
| Buttmann (2021) [3] | Germany | NA | Ocrelizumab | First line and switch | NR | 6-12 months | 1510 | Percentage of patients remaining relapse free | 93.3% | NA | NR | RMS patients |
| Butzkueven (2019) [28] | Europe and Australia | NA | Ocrelizumab | First line and switch | Various | >6 months (follow-up) | 234 | Number of patients who remained relapse free | 214 (91.5%) | 87.1-94.4 (95% CI) | NR | NA |
| Cellerino (2021) [39] | Italy | NA | Ocrelizumab | NR | NA | 2 years | 93 | Percentage of patients who remained relapse free | 95% | NA | NR | NA |
| | | | Ocrelizumab | NR | NA | 2 years | 93 | Number of patients with relapse | 4 (4%) | NA | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fernandez-Diaz (2021) [30] | Spain | NA | Ocrelizumab | First line, 36 and switch, 108 | Various | 10 months (median follow-up) | 136 | Number (and percentage) of patients who remained relapse free | 124 (91.2%) | NA | NR | NA |
| Garcia-Canibano (2021) [7] | Qatar | NA | Ocrelizumab | First line, 24 and switch, 36 | Various | 19.3 months (mean follow-up) | 57 | Number (and percentage) of patients with relapses | 10 (18%) | NA | NR | NA |
| | | | Ocrelizumab | First line, 24 and switch, 36 | Various | 19.3 months (mean follow-up) | 57 | Number (and percentage) of patients who remained relapse free | 47 (82%) | NA | NR | NA |
| Guerra (2021) [31] | Italy | NA | Ocrelizumab | NR | NA | 1.8 years (median follow up) | 76 | Number of patients with relapses | 0 (0%) | NA | NR | NA |
| Lopez Ruiz (2021) [9] | Spain | NA | Ocrelizumab | First line, 5 and switch, 47 | NR | 1 year | 52 | Number of patients with relapses | 1 (2%) | NA | NR | NA |
| Mancinelli (2020) [10] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 3 months | 42 | Number (and | 2 (5%) | NA | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | percentage) of patients with relapses | | | | |
| | | | Ocrelizumab | Switch | Natalizumab | 3-6 months | 42 | Number (and percentage) of patients with relapses | 0 (0%) | NA | NR | NA |
| Neo (2020) [11] | England | NA | Ocrelizumab | First line (15%) and switch | Various | 4.8 months | 170 | Number (and percentage) of patients with relapses | 12 (7.1%) | NA | NR | NA |
| Pasanisi (2020) [12] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 4 months | 42 | Number of patients with relapses | 4 (10%) | NA | NR | NA |
| Rojas (2021) [35] | Argentina, Chile, Mexico | NA | Ocrelizumab | First-line, 7 and switch, 45 | Various | Baseline | 52 | Number (and percentage) of patients with relapses | 32 (62%) | NA | NR | NA |
| | | | Ocrelizumab | First-line, 7 and switch, 45 | Various | >1 year | 52 | Number (and percentage) of patients | 8 (15%) | NA | 0.01 | Compared to baseline |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | with relapses | | | | |
| Rolfes (2021) [13] | Germany | Standard interval dosing | Ocrelizumab | First line, 38 and switch, 164 | NR | Baseline | 202 | Number (and percentage) of patients with relapse | 14 (6.9%) | NA | NR | NA |
| | | Extended interval dosing | Ocrelizumab | First line, 24 and switch, 92 | NR | Baseline | 116 | Number (and percentage) of patients with relapse | 9 (7.8%) | NA | NR | NA |
| | | Standard interval dosing | Ocrelizumab | First line, 38 and switch, 164 | NR | 3 months following third dose of ocrelizumab | 202 | Number (and percentage) of patients with relapse | 20 (9.9%) | NA | NR | NA |
| | | Extended interval dosing | Ocrelizumab | First line, 24 and switch, 92 | NR | 3 months following third dose of ocrelizumab | 116 | Number (and percentage) of patients with relapse | 11 (9.5%) | NA | NR | NA |
| Treffts (2021) [15] | Germany, Denmark | NA | Ocrelizumab | Switch | Natalizumab | 6 months | 196 | Number (and percentage) of patients | 16 (8.2%) | NA | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | with relapses | | | | |
| | | | Cladribine | Switch | Natalizumab | 6 months | 27 | Number (and percentage) of patients with relapses | 4 (15%) | NA | NR | NA |
| Van Kesteren (2021) [16] | Germany, Norway, Denmark | NA | Ocrelizumab | Switch | Fingolimod | 6 months | 196 | Number (and percentage) of patients with relapses | 18 (9.2%) | NA | NR | NA |
| | | | Cladribine | Switch | Fingolimod | 6 months | 58 | Number (and percentage) of patients with relapses | 11 (19%) | NA | NR | NA |
| Zanghi (2021) [17] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 18 months (median follow-up) | 64 | Number (and percentage) of patients with relapses | 5 (8%) | NA | NR | NA |
| | | | Rituximab | Switch | Natalizumab | 17 months (median follow-up) | 36 | Number (and percentage) of patients | 5 (14%) | NA | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | with relapses | | | | |
| | | | Cladribine | Switch | Natalizumab | 16 months (median follow-up) | 20 | Number (and percentage) of patients with relapses | 4 (20%) | NA | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 18 months (median follow-up) | 64 | Number (and percentage) of patients with more than one relapse | 0 (0%) | NA | 0.017 | Between treatments |
| | | | Rituximab | Switch | Natalizumab | 17 months (median follow-up) | 36 | Number (and percentage) of patients with more than one relapse | 3 (8%) | NA | 0.017 | Between treatments |
| | | | Cladribine | Switch | Natalizumab | 16 months (median follow-up) | 20 | Number (and percentage) of patients with more than one relapse | 3 (15%) | NA | 0.017 | Between treatments |
| Zhong (2021) [18] | Global | NA | None | Switch | Various | During washout | 1,096 | Number (and | 45 (4.1%) | NA | 0.037 | Fingolimod compared |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | (mean 44.3 days) | | percentage) of patients with relapses | | | | to other prior DMTs |
| | | <1 month washout | None | Switch | Various | During washout | 497 | Number (and percentage) of patients with relapses | 2 (0.4%) | NA | <0.001 | 2-6 month group vs 1-2 month and <1 month groups |
| | | 1-2 months washout | None | Switch | Various | During washout | 400 | Number (and percentage) of patients with relapses | 16 (4.0%) | NA | <0.001 | 2-6 month group vs 1-2 month and <1 month groups |
| | | 2-6 months washout | None | Switch | Various | During washout | 199 | Number (and percentage) of patients with relapses | 27 (15.7%) | NA | <0.001 | 2-6 month group vs 1-2 month and <1 month groups |
| | | NA | Ocrelizumab | Switch | Various | < 1 year | 1,096 | Number (and percentage) of patients with relapses | 47 (4.3%) | NA | 0.002 | Fingolimod compared to other prior DMTs |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | <1 month washout | Ocrelizumab | Switch | Various | < 1 year | 497 | Percentage of patients with relapse | 2.8% | NA | 0.066 | Comparison of survival curves between washout groups |
| | | 1-2 months washout | Ocrelizumab | Switch | Various | < 1 year | 400 | Percentage of patients with relapse | 5.3% | NA | 0.066 | Comparison of survival curves between washout groups |
| | | 2-6 months washout | Ocrelizumab | Switch | Various | < 1 year | 199 | Percentage of patients with relapse | 6.0% | NA | 0.066 | Comparison of survival curves between washout groups |
| **Primary progressive MS** | | | | | | | | | | | | |
| Rojas (2021) [35] | Argentina, Chile, Mexico | NA | Ocrelizumab | First line, 12 and switch | Various | Baseline | 29 | Number (and percentage) of patients with relapse activity | 11 (38%) | NA | NR | NA |
| | | | Ocrelizumab | First line, 12 and switch | Various | >1 year | 29 | Number (and percentage) of patients | 2 (7%) | NA | 0.37 | Baseline vs follow-up |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | with relapse activity | | | | |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | | | | | |
| Ellwardt (2020) [40] | Germany | NA | Ocrelizumab | First line (24%) and switch (76%) | Various | 200 days (median follow-up) | 136 | Percentage of patients with relapse | 13% | NA | NR | All relapses were in RRMS patients |
| Moss (2019) [43] | NR | NA | Ocrelizumab | NR | NA | 6 months | 272 | Number of patients with relapse | 10 (3.7%) | NA | NR | NA |
| Pontieri (2022) [33] | Denmark | NA | Ocrelizumab | First line, 174 and switch, 930 | Various | NR | 1104 | Number (and percentage) of patients with relapse | 102 (9.3%) | NA | NR | Study population includes patients with SPMS |
| Prockl (2020) [34] | Germany | NA | Ocrelizumab | First line, 5 and switch, 42 | Various | NR | 128 | Number of patients with relapse | 4 (3.1%) | NA | NR | NA |
| Signoriello (2022) [36] | Italy | Washout >12 weeks | Ocrelizumab | Switch | Fingolimod | Washout | 39 | Number (and percentage) of patients with relapse | 16 (41%) | NA | NR | NA |
| | | Washout 6-12 weeks | Ocrelizumab | Switch | Fingolimod | Washout | 39 | Number (and percentage) of | 5 (12.8%) | NA | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | patients with relapse | | | | |
| | | Washout <6 weeks | Ocrelizumab | Switch | Fingolimod | Washout | 25 | Number (and percentage) of patients with relapse | 5 (20%) | NA | NR | NA |
| | | NA | Ocrelizumab | Switch | Fingolimod and natalizumab | 6 months | 159 | Number (and percentage) of patients with relapse | 10 (6.3%) | NA | NR | NA |
| Smoot (2018) [46] | USA | NA | Ocrelizumab | First-line, 53 and switch, 170 | Various | NR | 223 | Number of patients with relapse | 7 (3.1%) | NA | NR | NA |
| Smoot (2021) [45] | USA | NA | Ocrelizumab | First line, 96 and switch, 126 | Various | 2 years | 332 | Number (and percentage) of patients with relapse | 33 (9.9%) | NA | NR | NA |
| Tsantes (2020) [48] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 6 months | 23 | Number of patients with relapse | 4 (17%) | NA | NR | NA |
| Van Lierop (2021) [49] | Netherlands | NA | Ocrelizumab | First line (n=39) and | Various | 45 weeks (median follow-up) | 165 | Number (and percentag | 0 (0%) | NA | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | switch (n=126) | | | | e) of patients with relapse | | | | |
| Vollmer (2019) [51] | USA | NA | Ocrelizumab | NR | NA | 1 year | 357 | Number of patients with relapse | 9 (2.5%) | NA | <0.001<br>0.638<br>0.225 | Ocrelizumab vs fingolimod and dimethyl fumarate, rituximab, natalizumab |
| Vollmer (2021) [50] | USA | NA | Ocrelizumab | NR | NA | NR | 245 | Number of patients with relapse | 4 (1.6%) | NA | NR | NA |

Abbreviations: CI, confidence interval; MS, multiple sclerosis; NA, not applicable; NR, not reported
[a]Some studies include patients with secondary progressive MS, but ≥80% of the total study population were RRMS and/or PPMS

## Supplementary Table 5. Studies reporting time to first relapse

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | | | | | |
| Bigaut (2022) [1] | France | NA | Ocrelizumab | Switch | Natalizumab | 1 year | 48 | Median time before first relapse (days) | 125 | 46-275 (IQR) | 0.4 | Ocrelizumab vs fingolimod |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 54 | Median time before first relapse (days) | 160 | 121-192 (IQR) | 0.4 | Ocrelizumab vs fingolimod |
| Frahm (2022) [6] | Germany | NA | Ocrelizumab | Switch | Fingolimod | NR | 33 | Median time to first relapse (months) | 2.7 | 0.6-8.2 (IQR) | NR | NA |
| Zanghi (2021) [17] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 18 months (median follow-up) | 64 | Median time to first relapse (months) | 3 | 2-3 (IQR) | NR | NA |
| | | | Rituximab | Switch | Natalizumab | 17 months (median follow-up) | 36 | Median time to first relapse (months) | 6 | 3-8 (IQR) | NR | NA |
| | | | Cladribine | Switch | Natalizumab | 16 months (media | 20 | Median time to first | 3 | 2.7-3.7 (IQR) | NR | NA |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | n follow-up) | | relapse (months) | | | | |
| Zhong (2021)[18] | Global | NA | None | Switch | Various | NR | 1,096 | Median time to first relapse (days) | 80 | 34-167.5 (IQR) | NR | NA |
| | | | Ocrelizumab | Switch | Injectable therapies | NR | 134 | Median time to first relapse (days) | 167 | NR | NR | NA |
| | | | Ocrelizumab | Switch | Dimethyl fumarate | NR | 128 | Median time to first relapse (days) | 171 | 111.5-232.25 (IQR) | NR | NA |
| | | | Ocrelizumab | Switch | Teriflunomide | NR | 74 | Median time to first relapse (days) | NA | NR | NR | NA |
| | | | Ocrelizumab | Switch | Fingolimod | NR | 411 | Median time to first relapse (days) | 52.5 | 28-119 (IQR) | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | NR | 349 | Median time to first relapse (days) | 108.5 | 77-212.75 (IQR) | NR | NA |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | | | | | |

| Author (year) | Country | Patient subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pontieri (2022) [33] | Denmark | NA | Ocrelizumab | First line, 174 and switch, 930 | Various | NA | 1104 | Median time to first relapse (months) | 4.2 | 1.8-9.3 (IQR) | NR | Study population includes patients with SPMS |
| Smoot (2021) [45] | USA | NA | Ocrelizumab | Switch | Natalizumab | NA | 66 | Median time to first relapse (months) | 8.7 | 3.3-13.9 (IQR) | NR | NA |
| Toorop (2021) [47] | Netherlands | NA | Ocrelizumab | NR | NR | NA | 117 | Time since last clinical relapse (years) | 2.7 | 2.1-4.8 (IQR) | NR | NA |

Abbreviations: IQR, interquartile range; MS, multiple sclerosis; NA, not applicable; NR, not reported
[a]Some studies include patients with secondary progressive MS, but ≥80% of the total study population were RRMS and/or PPMS

## Supplementary Table 6. Studies reporting annualized relapse rate

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | | | | | |
| Bigaut (2022) [1] | France | NA | Ocrelizumab | Switch | Natalizumab | Baseline | 48 | Mean number of relapses | 0.15 | 0.36 (SD) | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 1 year | 48 | Mean number of relapses | 0.12 | 0.39 (SD) | 0.035 | Ocrelizumab vs fingolimod |
| | | | Fingolimod | Switch | Natalizumab | Baseline | 54 | Mean number of relapses | 0.29 | 0.62 (SD) | NR | NA |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 54 | Mean number of relapses | 0.41 | 0.71 (SD) | 0.035 | Ocrelizumab vs fingolimod |
| Braune (2020) [27] | Germany | NA | Ocrelizumab | First line and switch | Fingolimod and natalizumab | >3 months | 439 | Mean ARR | 0.13 | 0.09-0.16 (95% CI) | NR | NA |
| Butzkueven, 2021 [38] | Australia, Turkey, Kuwait, Belgium | NA | Ocrelizumab | First line (13%) and switch) | Fingolimod and natalizumab | NR | 800 | ARR | 0.073 | 0.059-0.089 (95% CI) | NR | NA |
| Cellerino (2021) [39] | Italy | NA | Ocrelizumab | NR | NR | Baseline | 93 | Mean ARR | 0.78 | 0.70 (SD) | NR | NA |
| | | | Ocrelizumab | NR | NR | 1 year | 93 | Mean ARR | 0.04 | 0.18 (SD) | NR | NA |
| | | | Ocrelizumab | NR | NR | 2 years | 93 | Mean ARR | 0.04 | 0.21 (SD) | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Coban (2021) [29] | USA | NA | Ocrelizumab | First line, 25 and switch, 34 | NR | Baseline | 59 | Mean ARR | 1.4 | 0.9 (SD) | NR | NA |
| | | | Ocrelizumab | First line, 25 and switch, 34 | NR | Follow up | 59 | Mean ARR | 0.15 | NR | NR | NA |
| Fernandez-Diaz (2021) [30] | Spain | NA | Ocrelizumab | First line, 36 and switch, 108 | Various | Baseline | 144 | Mean ARR | 1.12 | 0.77 (SD) | NR | NA |
| | | | Ocrelizumab | First line, 36 and switch, 108 | Various | 10 months (median follow-up) | 144 | Mean ARR | 0.10 | 0.05-0.18 (95% CI) | NR | NA |
| Frahm (2022) [6] | Germany | NA | Ocrelizumab | Switch | Fingolimod | Baseline | 178 | ARR | 0.32 | NR | NR | NA |
| | | | Ocrelizumab | Switch | Fingolimod | Follow up | 178 | ARR | 0.15 | NR | NR | NA |
| Garcia-Canibano (2021) [7] | Qatar | NA | Ocrelizumab | First line, 24 and switch, 36 | Various | 19.3 months (median follow-up) | 57 | Mean ARR | 0.21 | 0.10-0.46 (95% CI) | NR | NA |
| Lopez Ruiz (2021) [9] | Spain | NA | Ocrelizumab | First line, 5 and switch, 47 | NR | Baseline | 52 | Median ARR | 1 | NR | NR | NA |
| | | | Ocrelizumab | First line, 5 and switch, 47 | NR | 19 months (mean follow-up) | 52 | Median ARR | 0 | NR | NR | NA |
| Mancinelli | Italy | NA | Ocrelizumab | Switch | Natalizumab | Baseline | 42 | Median ARR | 0 | NR | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (2020) [10] | | | Ocrelizumab | Switch | Natalizumab | 6 months | 42 | Median ARR | 0 | 0-2 (range) | NR | NA |
| Pontieri (2022) [33] | Denmark | NA | Ocrelizumab | First line, 118 and switch, 828 | Various | 1 year prior | 946 | Mean ARR | 0.63 | 0.59-0.68 (95% CI) | NR | NA |
| | | | Ocrelizumab | First line, 118 and switch, 828 | Various | Whole treatment period | 944 | Mean ARR | 0.09 | 0.08-0.12 (95% CI) | NR | NA |
| | | | Ocrelizumab | First line, 118 and switch, 828 | Various | First 6 months of treatment | 944 | Mean ARR | 0.16 | 0.12-0.20 (95% CI) | NR | NA |
| | | | Ocrelizumab | First line, 118 and switch, 828 | Various | 6 months after start of treatment until end of follow-up | 798 | Mean ARR | 0.05 | 0.04-0.08 (95% CI) | NR | NA |
| Rojas (2021) [35] | Argentina, Chile, Mexico | NA | Ocrelizumab | First-line, 7 and switch, 45 | Various | Baseline | 52 | Mean relapse rate | 1.4 | 0.7 (SD) | NR | NA |
| | | | Ocrelizumab | First-line, 7 and switch, 45 | Various | >1 year | 52 | Mean relapse rate | 0.23 | 0.4 (SD) | <0.001 | Compared to baseline |
| Semper e (2020) [44] | Spain | NA | Ocrelizumab | First line, 10 and switch, 39 | Various | Baseline | 49 | Mean ARR | 1.3 | 0.65 (SD) | NR | NA |
| | | | Ocrelizumab | First line, 10 and switch, 39 | Various | 2 years | 49 | Mean ARR | 0.02 | 0.14 (SD) | <0.001 | Baseline vs follow-up RMS patients |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Smoot (2021)[45] | USA | NA | Ocrelizumab | First line, 59 and switch, 217 | Various | Baseline | 278 | Mean ARR | 0.34 | 0.42 (SD) | NR | RMS patients |
| | | | Ocrelizumab | First line, 59 and switch, 217 | Various | 2 years | 278 | Mean ARR | 0.09 | NR | NR | RMS patients |
| Zanghi (2021)[17] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 18 months (median follow-up) | 64 | Mean ARR | 0.001 | NR | 0.053 | Between treatments |
| | Italy | NA | Rituximab | Switch | Natalizumab | 17 months (median follow-up) | 36 | Mean ARR | 0.308 | NR | 0.053 | Between treatments |
| | Italy | NA | Cladribine | Switch | Natalizumab | 16 months (median follow-up) | 20 | Mean ARR | 0.5 | NR | 0.053 | Between treatments |
| **Primary progressive MS** | | | | | | | | | | | | |
| Rojas (2021)[35] | Argentina, Chile, Mexico | NA | Ocrelizumab | First line, 12 and switch | Various | Baseline | 29 | Mean relapse rate | 1.00 | 0.30 | NR | NA |
| | | | Ocrelizumab | First line, 12 and switch | Various | >1 year | 29 | Mean relapse rate | 0.22 | 0.15 (SD) | 0.01 | Baseline vs follow-up |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | | | | | |
| Pontieri (2022)[33] | Denmark | NA | Ocrelizumab | First line (n=174) and switch (n=930) | Various | Baseline (1 year prior) | 1104 | Mean ARR | 0.58 | 0.53-0.62 (95% CI) | NR | Study population includes patients with SPMS |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Ocrelizumab | First line (n=174) and switch (n=930) | Various | 1 year treatment period | 1102 | Mean ARR | 0.09 | 0.07-0.11 (95% CI) | NR | NA |
| | | | Ocrelizumab | First line (n=174) and switch (n=930) | Various | First 6 months of treatment | 1102 | Mean ARR | 0.14 | 0.11-0.18 (95% CI) | NR | NA |
| | | | Ocrelizumab | First line (n=174) and switch (n=930) | Various | Second 6 months of treatment | 936 | Mean ARR | 0.06 | 0.04-0.07 (95% CI) | NR | NA |
| Signoriello (2022) [36] | Italy | NA | Ocrelizumab | Switch | Fingolimod and natalizumab | Washout | 165 | Mean ARR | 0.78 | 0.14 (SD) | 0.025 | Patients previously treated with fingolimod vs natalizumab |
| | | NA | Ocrelizumab | Switch | Fingolimod and natalizumab | 6 months | 159 | Mean ARR | 0.14 | 0.053-0.22 (95% CI) | 0.77 | Patients previously treated with fingolimod vs natalizumab |
| | | Switched from fingolimod | Ocrelizumab | Switch | Fingolimod | Baseline | 110 | Mean ARR | 0.57 | 0.68 (SD) | NR | NA |
| | | Switched from fingolimod | Ocrelizumab | Switch | Fingolimod | 6 months | 110 | Mean ARR | NR | NR | <0.001 | Compared to previous year |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Switched from natalizumab | Ocrelizumab | Switch | Natalizumab | Baseline | 55 | Mean ARR | 0.25 | 0.70 (SD) | NR | NA |
| | | Switched from natalizumab | Ocrelizumab | Switch | Natalizumab | 6 months | 55 | Mean ARR | NR | NR | 0.36 | Compared to previous year |

Abbreviations: ARR, annualized relapse rate; CI, confidence interval; MS, multiple sclerosis; NA, not applicable; NR, not reported; OR, odds ratio; SD, standard deviation
[a]Some studies include patients with secondary progressive MS, but ≥80% of the total study population were RRMS and/or PPMS

## Supplementary Table 7. Studies reporting magnetic resonance imaging activity

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | | | | | | |
| Bigaut (2022)[1] | France | NA | Ocrelizumab | Switch | Natalizumab | 3-6 months after initiation | 31 | Number & % of patients with ≥1 GdE lesion | NR | 0 (0%) | NA | 0.5 | Ocrelizumab vs fingolimod |
| | | | Fingolimod | Switch | Natalizumab | 3-6 months after initiation | 33 | Number & % of patients with ≥1 GdE lesion | NR | 2 (6%) | NA | 0.5 | Ocrelizumab vs fingolimod |
| | | | Ocrelizumab | Switch | Natalizumab | 3-6 months after initiation | 33 | Number & % of patients ≥1 new T2-lesion | NR | 0 (0%) | NA | 0.02 | Ocrelizumab vs fingolimod |
| | | | Fingolimod | Switch | Natalizumab | 3-6 months after initiation | 30 | Number & % of patients ≥1 new T2-lesion | NR | 5 (17%) | NA | 0.02 | Ocrelizumab vs fingolimod |
| | | | Ocrelizumab | Switch | Natalizumab | 1 year | 19 | Number & % of patients ≥1 new T2-lesion | NR | 1 (5%) | NA | 0.36 | Ocrelizumab vs fingolimod |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 24 | Number & % of patients ≥1 new T2-lesion | NR | 4 (17%) | NA | 0.36 | Ocrelizumab vs fingolimod |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cellerino (2021)[39] | Italy | RRMS | Ocrelizumab | NR | NR | 2 years | 93 | % of patients free of MRI disease activity | NR | 67% | NA | NR | NA |
| | | | | | | 2 years + 100-day re-baseline | 93 | % of patients free of MRI disease activity | NR | 82% | NA | NR | NA |
| | | | | | | 2 years + 180-day re-baseline | 93 | % of patients free of MRI disease activity | NR | 92% | NA | NR | NA |
| Coban (2021)[29] | USA | RRMS | Ocrelizumab | First line, 25 (42%) Switch, 34 (58%) | NR | NR | 59 | Mean number of patients with new/enlarging T2 lesions | NR | 10 (17%) | 5 (SD) | NR | NA |
| Fernandez-Diaz (2021)[30] | Spain | RRMS | Ocrelizumab | First-line, 36 (25%) Switch, 108 (75%) | Various | 12 months | 44 | Number & % of patients with MRI activity | NR | 3 (7%) | NA | NR | NA |
| | | | | | | | | Number & % of patients with GdE | NR | 1 (2%) | NA | NR | NA |
| | | | | | | | | Number & % of patients | NR | 3 (7%) | NA | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | with new T2 lesions | | | | | |
| Garcia-Canibano (2021)[7] | Qatar | NA | Ocrelizumab | First line, 24 Switch, 36 | Various | 12 months | 57 | Number and % of patients with presence of one or more T1 GdE | NR | 4 (8%) | NA | NR | NA |
| Lopez Ruiz (2021)[9] | Spain | NA | Ocrelizumab | First line, 5 Switch, 47 | NR | Mean follow-up: 19 months (SD 15.1) | 52 | MRI activity, GdE | 1.4 | 0 (0%) | NA | NR | NA |
| Mancinelli (2020)[10] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 3 months | 42 | Number and % of patients with MRI activity | NR | 4 (10%) | NA | NR | NA |
| | | | | | | 6 months | 42 | Number and % of patients with MRI activity | NR | 4 (10%) | NA | NR | NA |
| Pasanisi (2020)[12] | Italy | NA | Ocrelizumab | Switch | Various | 3 months | 42 | Number of patients with new/enlarging GdE lesions | NR | 1 (2%) | NA | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 12 months | 42 | Number of patients with new/enlarging T2 lesions | NR | 4 (10%) | NA | NR | NA |
| Rojas (2021)[35] | Argentina, Chile, Mexico | RRMS | Ocrelizumab | First-line, 12 (42%) and switch | Various | 12 months | 52 | Number & % of patients with GdE | 30 (58%) | 4 (8%) | NA | 0.06 | Baseline vs 12 months |
| | | | | | | | | Number & % of patients with T2 MRI activity | 41 (79%) | 18 (35%) | NA | 0.001 | Baseline vs 12 months |
| Rolfes (2021)[13] | Germany | Standard interval dosing | Ocrelizumab | First line, 38 (20.1%) Switch, 164 (79.9%) | NR | Follow-up | 202 | Number and % of patients with MRI progression | 24 (11.9%) | 9 (4.5%) | NA | NA | NA |
| | | Extended interval dosing | Ocrelizumab | First line, 24 (21.3%) Switch, 92 (78.7%) | NR | Follow-up | 116 | Number and % of patients with MRI progression | 11 (9.5%) | 8 (6.9%) | NA | NA | NA |
| Signoriello (2022)[36] | Italy | All patients | Ocrelizumab | Switch | Fingolimod, 110 Natalizumab, 55 | 6 months | 159 | Number of patients with GdE | NR | 2 (1.3%) | NA | NR | NA |
| Smoot (2021)[14] | NR | NR | Ocrelizumab | Switch | Natalizumab | 3 months | 43 | Number of patients with new enhancing | NR | 2 (5%) | NA | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | lesions on MRI | | | | | |
| | | | | | | 3 months | 43 | Number of patients with new T2 hyperintensity on MRI | NR | 2 (5%) | NA | | NA |
| | | | | | | 3-6 months | 43 | Number of patients with new enhancing lesions on MRI | NR | 0 (0%) | NA | NR | NA |
| | | | | | | 3-6 months | 43 | Number of patients with new T2 hyperintensity on MRI | NR | 0 (0%) | NA | NR | NA |
| | | | | | | 6-12 months | 43 | Number of patients with new enhancing lesions on MRI | NR | 0 (0%) | NA | NR | NA |
| | | | | | | 6-12 months | 43 | Number of patients with new T2 hyperintensity on MRI | NR | 0 (0%) | NA | NR | NA |
| Zanghi (2021)[17] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 6 months | 64 | Number & % of patients with | NR | 5 (8%) | NA | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | increased lesions | | | | | |
| | | | | | | 12 months | 64 | Number & % of patients with increased lesions | NR | 3 (8%) | NA | NR | NA |
| | | | Rituximab | Switch | Natalizumab | 6 months | 36 | Number & % of patients with increased lesions | NR | 4 (20%) | NA | NR | NA |
| | | | | | | 12 months | 36 | Number & % of patients with increased lesions | NR | 6 (9%) | NA | NR | NA |
| | | | Cladribine | Switch | Natalizumab | 6 months | 20 | Number & % of patients with increased lesions | NR | 6 (17%) | NA | NR | NA |
| | | | | | | 12 months | 20 | Number & % of patients with increased lesions | NR | 4 (20%) | NA | NR | NA |
| **Primary progressive MS** | | | | | | | | | | | | | |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cellerino (2021)[39] | Italy | PPMS | Ocrelizumab | NR | NR | 2 years | 43 | % of patients free of MRI evidence of disease activity | NR | 81% | NA | NR | NA |
| | | | | | | 2 years + 100-day re-baseline | 43 | % of patients free of MRI evidence of disease activity | NR | 84% | NA | NR | NA |
| | | | | | | 2 years + 180-day re-baseline | 43 | % of patients free of MRI evidence of disease activity | NR | 88% | NA | NR | NA |
| Coban (2021)[29] | USA | PPMS | Ocrelizumab | First line, 11 (79%) Switch, 3 (21%) | NR | NR | 14 | Mean number of patients with new/enlarging T2 lesions | NR | 10 (71%) | 5 (SD) | NR | NA |
| Fernandez-Diaz (2021)[30] | Spain | PPMS | Ocrelizumab | First-line, 46 (78%) Switch, 13 (22%) | Various | 12 months | 45 | Number & % of patients with MRI activity | NR | 4 (9%) | NA | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Number & % of patients with GdE | NR | 2 (4%) | NA | NR | NA |
| | | | | | | | | Number & % of patients with new T2 lesions | NR | 2 (4%) | NA | NR | NA |
| Rojas (2021) [35] | Argentina, Chile, Mexico | PPMS | Ocrelizumab | First-line, 12 (42%) and switch | Various | 12 months | 29 | Number & % of patients with GdE | 10 (34.5 %) | 2 (7%) | NA | 0.44 | Baseline vs 12 months |
| | | | | | | | | Number & % of patients with T2 MRI activity | 19 (65.5 %) | 7 (24% ) | NA | 0.05 | Baseline vs 12 months |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | | | | | | |
| Pontieri (2022) [33] | Denmark | NA | Ocrelizumab | First line, 174 (15.8%) Switch, 930 (84.2%) | Various | Baseline (within 6 months prior to ocrelizumab initiation) | 836 | Number and % of patients with radiological disease activity | NR | 302 (36.1 %) | 32.9-39.5 (95% CI) | NR | NR |
| | | | | | | Re-baseline (first scan | 808 | Number and % of patients with | NR | 154 (19.1 %) | 16.4-21.9 (95% CI) | NR | NR |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | after ocrelizumab initiation. Median 4.1 months (IQR 2.8-5.5)) | | radiological disease activity | | | | | |
| | | | | | | First scan after re-baseline. Median 7.5 months (IQR 5.5-11.7) | 363 | Number and % of patients with radiological disease activity | NR | 20 (5.5 %) | 3.4-8.4 (95% CI) | NR | NR |
| Sempere (2021)[44] | Spain | NA | Ocrelizumab | First-line and switch | Various | 4-6 months | 70 | Number and % of patients with GdE | 40 (57%) | 1 (1%) | NA | <0.001 | Baseline vs 4-6 months |
| | | | | | | 12 months | 70 | Number and % of patients with GdE | 40 (57%) | 0 (0%) | NA | <0.001 | Baseline vs 12 months |
| | | | | | | 12 months | 70 | Number and % of patients with new or enlarging T2- | NR | 1/46 (2%) | NA | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | hyperintense lesions | | | | | |
| Smoot (2021) [45] | USA | NA | Ocrelizumab | First-line, 96 (27.4%) and switch | NR | Follow up | 291 | Number and % of patients with stable MRI | NR | 262 (90%) | NA | NR | NA |
| | | | | | | | | Number & % of patients with enhancing lesions | NR | 4 (1.4%) | NA | NR | NA |
| Toorop (2021) [47] | Netherlands | NA | Ocrelizumab | NR | NR | 1.7 years | 117 | Median time since last MRI disease activity | NA | 2 years | 1.4-1.6 (IQR) | NR | NA |
| | | | | | | | | Number and % of patients with MRI disease activity during treatment | NA | 35 (29.9%) | NA | NR | NA |
| Van Lierop (2021) [49] | Netherlands | NA | Ocrelizumab | First line, 39 (23.6%) Switch, 126 (76.4%) | Various | Median follow-up: 45 weeks (IQR: 38-51) | 107 | Number and % of patients with MRI activity without evidence of radiological | NR | 2 (1.9%) | NA | NA | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | disease activity on the previous MRI scan | | | | | |
| Vollmer (2019)[51] | USA | NA | Ocrelizumab | NR | NR | Up to one year | 357 | Number of patients with enhancing lesion | NR | 2 | NA | NR | NA |
| | | | | | | | | Number of patients with new T2 lesion | NR | 27 | NA | NR | NA |
| | | | | | | | | Odds of experiencing disease activity (clinical relapse, new T2 lesions, and/or contrast enhancing lesions) with fingolimod vs ocrelizumab | NR | 3.82 | NA | <0.001 | NA |
| | | | | | | | | Odds of experiencing disease activity | NR | 3.99 | NA | <0.001 | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | (clinical relapse, new T2 lesions, and/or contrast enhancing lesions) with dimethyl fumarate vs ocrelizumab | | | | | |
| | | | | | | | | Odds of experiencing disease activity (clinical relapse, new T2 lesions, and/or contrast enhancing lesions) with rituximab vs ocrelizumab | NR | 1.17 | NA | 0.638 | NA |
| | | | | | | | | Odds of experiencing disease activity (clinical relapse, new T2 lesions, and/or contrast | NR | 1.36 | NA | 0.225 | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Baseline value | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | enhancing lesions) with natalizumab vs ocrelizumab | | | | | |

Abbreviations: GdE, gadolinium-enhancing lesion; IQR, interquartile range; MRI, magnetic resonance imaging; 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

## Supplementary Table 8. Studies reporting expanded disability status scale scores

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | | | | | |
| Bigaut (2022) [1] | France | NA | Ocrelizumab | Switch | Natalizumab | Baseline | 48 | Mean EDSS | 2.4 | 1.7 (SD) | NR | NA |
| | | | Fingolimod | Switch | Natalizumab | Baseline | 54 | Mean EDSS | 2.8 | 1.7 (SD) | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 1 year | 48 | Mean EDSS | 2.3 | 1.7 (SD) | 0.18 | Ocrelizumab vs fingolimod |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 54 | Mean EDSS | 2.8 | 1.8 (SD) | 0.18 | Ocrelizumab vs fingolimod |
| Coban (2021) [29] | US | NA | Ocrelizumab | First line, 25 (42%) Switch, 34 (58%) | NR | Baseline | 29 | Mean EDSS | 2.20 | 1.00 (SD) | NR | NA |
| | | | Ocrelizumab | First line 25 (42%) Switch 34 (58%) | NR | NR | 29 | Mean EDSS | 2.17 | 1.22 (SD) | NR | NA |
| Frahm (2022) [6] | Germany | NA | Ocrelizumab | Switch | Fingolimod | Baseline | 101 | Median EDSS | 3.5 | NR | NR | NA |
| | | | Ocrelizumab | Switch | Fingolimod | 6-12 months | 101 | Median EDSS | 3.0 | NR | NR | NA |
| Garcia-Caniba no (2021) [7] | Qatar | NA | Ocrelizumab | First line, 24 (38%) Switch, 36 (62%) | Various | Baseline | 57 | Mean EDSS | 2.1 | 2.4 (SD) | NR | NA |
| | | | Ocrelizumab | First line, 24 (38%) Switch, 36 (62%) | Various | 12 months | 57 | Mean EDSS | 2.0 | 2 (IQR) | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Guerra (2021) [31] | Italy | NA | Ocrelizumab | NR | NA | Baseline | 76 | Mean EDSS | 4 | 1.0-7.5 (IQR) | NR | NA |
| | | | Ocrelizumab | NR | NA | 1.80 years (median follow-up) | 76 | Mean EDSS | 4 | 1.0-8.0 (SD) | NR | NA |
| Lanzillo (2021) [8] | Italy | NA | Ocrelizumab | NR | NR | 1 year | 89 | NR | NR | NA | <0.001 | Higher EDSS at baseline compared to follow-up |
| Lopez Ruiz (2021) [9] | Spain | NA | Ocrelizumab | First line, 5 Switch, 47 | NR | Baseline | 52 | Median EDSS | 3.5 | 1.5-6.5 (IQR) | NR | NA |
| | | | Ocrelizumab | First line, 5 Switch, 47 | NR | 19 months (mean follow-up) | 52 | Median EDSS | 2.5 | 1.5-6.5 (IQR) | NA | NA |
| Mancinelli (2020) [10] | Italy | NA | Ocrelizumab | Switch | Natalizumab | Baseline | 42 | Median EDSS | 3.0 | 0.0-8.0 (range) | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 6 months | 42 | Median EDSS | 3.0 | 0.0-8.0 (range) | NR | NA |
| Ozakbas (2021) [32] | NR | NA | Ocrelizumab | NR | NA | 6 months | 87 | NR | NR | NR | 0.102 | Baseline vs follow-up |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Smoot (2021) [45] | US | NA | Ocrelizumab | First-line, 59 Switch, 219 | Various | Baseline | 278 | Median EDSS | 3.0 | 2.0-4.0 (IQR) | NR | RMS patients |
| | | | Ocrelizumab | First-line, 59 Switch, 219 | Various | 12 months | 278 | Median EDSS | 3.0 | 2.0-5.5 (IQR) | NR | RMS patients |
| Smoot (2021) [14] | NR | NA | Ocrelizumab | Switch | Natalizumab | Baseline | 35 | Median EDSS | 3.5 | 2.25 (IQR) | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 12 months | 35 | Median EDSS | 3.5 | 2.00 (IQR) | NR | NA |
| Zanghi (2021) [17] | Italy | NA | Ocrelizumab | Switch | Natalizumab | Baseline | 64 | Median EDSS | 3.0 | 2.0-4.5 (IQR) | NR | NA |
| | | | Rituximab | Switch | Natalizumab | Baseline | 36 | Median EDSS | 4.0 | 2.0-4.5 (IQR) | NR | NA |
| | | | Cladribine | Switch | Natalizumab | Baseline | 20 | Median EDSS | 2.0 | 1.0-3.0 (IQR) | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 6 months | 64 | Median EDSS | 3.0 | 2.0-4.5 (IQR) | NR | NA |
| | | | Rituximab | Switch | Natalizumab | 6 months | 36 | Median EDSS | 4.0 | 2.0-4.5 (IQR) | NR | NA |
| | | | Cladribine | Switch | Natalizumab | 6 months | 20 | Median EDSS | 2.0 | 1.0-4.0 (IQR) | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 12 months | 64 | Median EDSS | 3.0 | 2.0-4.5 (IQR) | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Rituximab | Switch | Natalizumab | 12 months | 36 | Median EDSS | 3.5 | 1.5-4.0 (IQR) | NR | NA |
| | | | Cladribine | Switch | Natalizumab | 12 months | 20 | Median EDSS | 3.0 | 1.5-5.0 (IQR) | NR | NA |
| | | | Ocrelizumab | Switch | Natalizumab | 18 months | 64 | Median EDSS | 3.0 | 2.0-4.5 (IQR) | NR | NA |
| | | | Rituximab | Switch | Natalizumab | 18 months | 36 | Median EDSS | 3.5 | 1.5-4.0 (IQR) | NR | NA |
| | | | Cladribine | Switch | Natalizumab | 18 months | 20 | Median EDSS | 3.0 | 1.5-5.0 (IQR) | NR | NA |
| **Primary progressive MS** | | | | | | | | | | | | |
| Alcala (2022)[19] | Spain | NA | Rituximab | First-line, 19 Switch, 30 | NR | Baseline | 49 | Mean EDSS | 5.4 | 1.6 (SD) | NR | NA |
| | | | Ocrelizumab | First-line, 40 Switch, 6 | NR | Baseline | 46 | Mean EDSS | 4.7 | 1.3 (SD) | NR | NA |
| | | | Rituximab | First-line, 19 Switch, 30 | NR | Baseline | 49 | Median EDSS | 6.0 | 2-8 (range) | NR | NA |
| | | | Ocrelizumab | First-line, 40 Switch, 6 | NR | Baseline | 46 | Median EDSS | 4.5 | 3-7 (range) | NR | NA |
| | | | Rituximab | First-line, 19 Switch, 30 | NR | 18.3 months (mean follow-up) | 49 | Mean EDSS | 5.9 | 1.7 (SD) | NR | NA |
| | | | Ocrelizumab | First-line, 40 | NR | 18.3 months | 46 | Mean EDSS | 4.9 | 1.5 (SD) | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Switch, 6 | | (mean follow-up) | | | | | | |
| | | | Rituximab | First-line, 19<br>Switch, 30 | NR | 18.3 months (mean follow-up) | 49 | Median EDSS | 6 | 2-8.5 (range) | NR | NA |
| | | | Ocrelizumab | First-line, 40<br>Switch, 6 | NR | 18.3 months (mean follow-up) | 46 | Median EDSS | 4.5 | 2.5-7 (range) | NR | NA |
| Braune (2021) [20] | Germany | NA | Ocrelizumab | NR | NR | 1 year | 82 | EDSS | NR | NA | NR | No significant change in EDSS (baseline vs follow-up) |
| Coban (2021) [29] | US | NA | Ocrelizumab | First line, 11 (79%)<br>Switch, 3 (21%) | NR | Baseline | 9 | Mean EDSS | 4.6 | 1.5 (SD) | NR | NA |
| | | | Ocrelizumab | First line, 11 (79%)<br>Switch, 3 (21%) | NR | NR | 9 | Mean EDSS | 4.77 | 1.75 (SD) | NR | NA |
| Guerra (2021) [31] | Italy | NA | Ocrelizumab | NR | NR | Baseline | 35 | Median EDSS | 5.5 | 4-8 (IQR) | NR | NA |
| | | | Ocrelizumab | NR | NR | 2.09 years (median follow-up) | 35 | Mean EDSS | 6.5 | 4.5, 8.0 (SD) | 0.01 | Baseline vs follow-up |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Impellizzeri (2019)[22] | NA | NA | Ocrelizumab | NR | NR | Baseline | 54 | Median EDSS | 4.5 | 3-8 (range) | NR | NA |
| | | | Ocrelizumab | NR | NR | 1 year | 54 | Median EDSS | 5 | NA | NA | NA |
| Lopez Ruiz (2020)[23] | Spain | NA | Ocrelizumab | First-line, 12 (66.7%) Switch, 6 (33.3%) | Various | Baseline | 18 | Mean EDSS | 5.7 | NR | NR | NA |
| | | | Ocrelizumab | First-line, 12 (66.7%) Switch, 6 (33.3%) | Various | 13.8 months (mean follow-up) | 18 | Mean EDSS | 5.8 | NR | NR | NA |
| Ozakbas (2021)[32] | NR | NA | Ocrelizumab | NR | NR | 6 months | 42 | EDSS | NR | NR | 0.317 | Baseline vs follow-up |
| Smoot (2021)[45] | US | NA | Ocrelizumab | First line, 17 Switch, 13 | Various | Baseline | 30 | Median EDSS | 6.5 | 6-7 (IQR) | NR | NA |
| | | | Ocrelizumab | First line, 17 Switch, 13 | Various | 12 months | 30 | Median EDSS | 6.5 | 5.6-7.5 (IQR) | NR | NA |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | | | | | |
| Signoriello (2022)[36] | Italy | NA | Ocrelizumab | Switch | Fingolimod or natalizumab | Baseline | 165 | Median EDSS | 4.0 | 1.0-3.0 (IQR) | NR | NA |
| | | Switched from fingolimod | Ocrelizumab | Switch | Fingolimod | Baseline | 110 | Median EDSS | 4.5 | 2.5-6.5 (IQR) | NR | NA |
| | | Switched from | Ocrelizumab | Switch | Natalizumab | Baseline | 55 | Median EDSS | 3.0 | 1.5-5.5 (IQR) | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | natalizumab | | | | | | | | | | |
| | | Switched from fingolimod | Ocrelizumab | Switch | Fingolimod | 6 months | 110 | Delta reduction in EDSS | 0.07 | 0.53 (SD) | 0.41 | Baseline vs follow-up |
| | | Switched from natalizumab | Ocrelizumab | Switch | Natalizumab | 6 months | 55 | Delta reduction in EDSS | 0.10 | 0.6 (SD) | 0.91 | Baseline vs follow-up |
| Signoriello (2020) [37] | Italy | NA | Ocrelizumab | First (21.3%) Switch (78.7%) | Various | Baseline | 108 | Mean EDSS | 5.06 | 2.02 (SD) | NR | NA |
| | | | Ocrelizumab | First (21.3%) Switch (78.7%) | Various | 1 year | 108 | Mean EDSS | 4.46 | 2.23 (SD) | NR | NA |
| Toorop (2021) [47] | Netherlands | NA | Ocrelizumab | NR | NR | Baseline | 117 | Median EDSS | 3.5 | 2.5-5 (IQR) | NR | NA |
| | | | Ocrelizumab | NR | NR | 1.7 years (mean follow-up) | 117 | Median EDSS | 3.5 | 2.5-5.5 (IQR) | NR | NA |
| Van Lierop (2021) [49] | Netherlands | NA | Ocrelizumab | First line, 39 (23.6%) Switch, 126 (76.4%) | Various | Baseline | 96 | Median EDSS | 4 | 2.5-5 (IQR) | NR | NA |
| | | | Ocrelizumab | First line, 39 (23.6%) Switch, 126 (76.4%) | Various | 45 weeks (median follow-up) | 96 | Median EDSS | 4.0 | 3-6 (IQR) | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Yousuf (2021) [52] | Qatar | NA | Ocrelizumab | First-line (31.7%) Switch (68.3%) | NR | 2 years | 65 | Mean EDSS | 2.57 | 2.67 (SD) | NR | NA |

Abbreviations: 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

## Supplementary Table 9. Studies reporting disability worsening and/or improvement

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | | | | |
| Bigaut (2022) [1] | France | Patients with relapses at 1 year | Ocrelizumab | Switch | Natalizumab | 1 year | 5 | EDSS worsening, n (%) | 0 (0%) | 0.29 | Ocrelizumab vs fingolimod |
| | | Patients with relapses at 1 year | Fingolimod | Switch | Natalizumab | 1 year | 17 | EDSS worsening, n (%) | 5 (29%) | 0.29 | Ocrelizumab vs fingolimod |
| Butzkueven (2021) [38] | Australia, Turkey, Kuwait, Belgium | NA | Ocrelizumab | First line (13%) switch (87%) | Fingolimod (38.8%) and Natalizumab (27.8%) | 6 months | 800 | Number (and percentage) of patients with 1-point EDSS progression | 54 (6.8%) | NR | NA |
| | | | Ocrelizumab | First line (13%) switch (87%) | Fingolimod (38.8%) and Natalizumab (27.8%) | 6 months | 800 | Number (and percentage) of patients with 1-point EDSS regression | 58 (7.3%) | NR | NA |
| | | | Ocrelizumab | First line (13%) switch (87%) | Fingolimod (38.8%) and Natalizumab (27.8%) | 12 months | 800 | KM estimate of 6-month CDI at 12 months (percentage of patients) | 7.0% | NR | NA |
| | | | Ocrelizumab | First line (13%) switch (87%) | Fingolimod (38.8%) and Natalizumab (27.8%) | 24 months | 800 | KM estimate of 6-month CDI at 24 months (percentage of patients) | 10.3% | NR | NA |
| | | | Ocrelizumab | First line (13%) switch (87%) | Fingolimod (38.8%) and Natalizumab (27.8%) | 12 months | 800 | KM estimate of 6-month CDP free survival at 12 months | 96.3% | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | (percentage of patients) | | | |
| | | | Ocrelizumab | First line (13%) switch (87%) | Fingolimod (38.8%) and Natalizumab (27.8%) | 24 months | 800 | KM estimate of 6-month CDP free survival at 24 months (percentage of patients) | 90.7% | NR | NA |
| Cellerino (2021) [39] | Italy | NA | Ocrelizumab | NR | NR | 2 years | 93 | Percentage without disability worsening | 91% | NR | NA |
| Fernandez-Diaz (2021) [30] | Spain | NA | Ocrelizumab | First-line, 36 (25%) Switch, 108 (75%) | Various | 10 months (median follow-up) | 60 | EDSS improvement, n (%) | 12 (20%) | NR | NA |
| | | | Ocrelizumab | First-line, 36 (25%) Switch, 108 (75%) | Various | 10 months (median follow-up) | 60 | EDSS progression, n (%) | 2 (3%) | NR | NA |
| Garcia-Caniba no (2021) [7] | Qatar | NA | Ocrelizumab | First line, 24 (38%) Switch, 36 (62%) | Various | 12 months | 57 | EDSS improvement, n (%) | 4 (7%) | NA | NA |
| | | | Ocrelizumab | First line, 24 (38%) Switch, 36 (62%) | Various | 12 months | 57 | EDSS worsening, n (%) | 3 (5%) | NA | NA |
| Lopez Ruiz (2021) [9] | Spain | NA | Ocrelizumab | First line, 5 Switch, 47 | NR | 6 months | 52 | CDI | 19 (27%) | NA | NA |
| | | | Ocrelizumab | First line, 5 Switch, 47 | NR | 6 months | 52 | CDW | 2 (4%) | NA | NA |
| Mancinelli | Italy | NA | Ocrelizumab | Switch | Natalizumab | 3-6 months | 42 | Stable EDSS score, n (%) | 38 (90%) | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| (2020) [10] | | | | | | | | | | | |
| Neo (2020) [11] | England | NA | Ocrelizumab | First line (15%) Switch (85%) | Various | 6.5 months | 170 | Disability progression, n (%) | 27 (20%) | NA | NA |
| Pontieri (2022) [33] | Denmark | NA | Ocrelizumab | First line 118 (12.5%) Switch 828 (87.5%) | Various | 6 months | 946 | Percentage of patients with 24 week confirmed disability improvement | 13.0% | NR | NA |
| | | | Ocrelizumab | First line 118 (12.5%) Switch 828 (87.5%) | Various | 12 months | 946 | Percentage of patients with 24 week confirmed disability improvement | 17.1% | NR | NA |
| | | | Ocrelizumab | First line 118 (12.5%) Switch 828 (87.5%) | Various | 18 months | 946 | Percentage of patients with 24 week confirmed disability improvement | 17.8% | NR | NA |
| | | | Ocrelizumab | First line 118 (12.5%) Switch 828 (87.5%) | Various | 24 months | 946 | Percentage of patients with 24 week confirmed disability improvement | 17.8% | NR | NA |
| | | | Ocrelizumab | First line 118 (12.5%) Switch 828 (87.5%) | Various | 6 months | 946 | Percentage of patients with 24 week confirmed disability worsening | 4.1% | NR | NA |
| | | | Ocrelizumab | First line 118 (12.5%) Switch 828 (87.5%) | Various | 12 months | 946 | Percentage of patients with 24 week confirmed disability worsening | 7.2% | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Ocrelizumab | First line 118 (12.5%) Switch 828 (87.5%) | Various | 18 months | 946 | Percentage of patients with 24 week confirmed disability worsening | 7.8% | NR | NA |
| | | | Ocrelizumab | First line 118 (12.5%) Switch 828 (87.5%) | Various | 24 months | 946 | Percentage of patients with 24 week confirmed disability worsening | 7.8% | NR | NA |
| Rojas (2021) [35] | Argentina, Chile, Mexico | NA | Ocrelizumab | First-line, 7 (14%) Switch, 45 (86%) | Various | >1 year | 52 | EDSS progression, n (%) | 2 (4%) | 0.31 | Baseline vs follow-up |
| Rolfes (2021) [13] | Germany | Standard interval dosing | Ocrelizumab | First line, 38 (20.1%) Switch, 164 (79.9%) | NR | Baseline | 202 | CDP | 10 (5.0%) | NA | NA |
| | | Extended interval dosing | Ocrelizumab | First line, 24 (21.3%) Switch, 92 (78.7%) | NR | Baseline | 116 | CDP | 6 (5.2%) | NA | NA |
| | | Standard interval dosing | Ocrelizumab | First line, 38 (20.1%) Switch, 164 (79.9%) | NR | 3 months after last dose | 202 | CDP | 18 (8.9%) | NA | NA |
| | | Extended interval dosing | Ocrelizumab | First line, 24 (21.3%) Switch, 92 (78.7%) | NR | 3 months after last dose | 116 | CDP | 11 (9.5%) | NA | NA |
| Sempere (2020) [44] | Spain | NA | Ocrelizumab | NR | Various | 12 months | 49 | EDSS progression | 0 (0%) | NR | RMS patients |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Zanghi (2021) [17] | Italy | NA | Ocrelizumab | Switch | Natalizumab | 18 months (median follow-up) | 64 | CDP | 5 (8%) | NR | NA |
| | | | Rituximab | Switch | Natalizumab | 17 months (median follow-up) | 36 | CDP | 3 (8%) | NR | NA |
| | | | Cladribine | Switch | Natalizumab | 16 months (median follow-up) | 20 | CDP | 2 (10%) | NR | NA |
| Zhong (2021) [18] | Global | NA | Ocrelizumab | Switch | Various | 6 months | 513 | CDP | 18 (3.5%) | NA | NA |
| | | <1 month washout | Ocrelizumab | Switch | Various | 6 months | 215 | CDP | 0.9% | <0.001 | Comparison of survival curve estimates between washout groups |
| | | 1-2 months washout | Ocrelizumab | Switch | Various | 6 months | 203 | CDP | 3.4% | <0.001 | Comparison of survival curve estimates between washout groups |
| | | 2-6 months washout | Ocrelizumab | Switch | Various | 6 months | 95 | CDP | 10% | <0.001 | Comparison of survival curve estimates between washout groups |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Primary progressive MS** | | | | | | | | | | | |
| Cellerino (2021) [39] | Italy | NA | Ocrelizumab | NR | NR | 2 years | 43 | Free from disability worsening | 65% | NR | NA |
| Daniels (2020) [21] | Netherlands | NA | Ocrelizumab | NR | NA | NR | 21 | Improvement in disability status (EDSS) | 3 (14%) | NR | NA |
| | | | Ocrelizumab | NR | NA | NR | 21 | Disability progression rate per 12 weeks | -0.06 | NR | NA |
| | | | Ocrelizumab | NR | NA | NR | 21 | Disability progression rate per 12 weeks | 0.09 | NR | NA |
| Fernandez-Diaz (2021) [30] | Spain | NA | Ocrelizumab | First-line, 46 (78%) Switch, 13 (22%) | Various | 19 months (median follow-up) | 48 | EDSS improvement, n (%) | 4 (8%) | NR | NA |
| | | | Ocrelizumab | First-line, 46 (78%) Switch, 13 (22%) | Various | 19 months (median follow-up) | 48 | EDSS progression, n (%) | 18 (38%) | NR | NA |
| Pereira Coutinho (2021) [26] | NR | Control group | Ocrelizumab | NR | NR | 19 months (median follow-up) | 16 | EDSS progression, n (%) | 5 (31%) | NR | NA |
| | | Expanded group | Ocrelizumab | NR | NR | 19 months (median follow-up) | 35 | EDSS progression, n (%) | 12 (34%) | NR | NA |
| Pontieri (2022) [33] | Denmark | NA | Ocrelizumab | First line 48 (78.7%) Switch 13 (21.3%) | Various | 6 months | NR | Percentage of patients with 24 week confirmed disability improvement | 6.7% | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Ocrelizumab | First line 48 (78.7%) Switch 13 (21.3%) | Various | 12 months | NR | Percentage of patients with 24 week confirmed disability improvement | 10.3% | NR | NA |
| | | | Ocrelizumab | First line 48 (78.7%) Switch 13 (21.3%) | Various | 18 months | NR | Percentage of patients with 24 week confirmed disability improvement | 10.3% | NR | NA |
| | | | Ocrelizumab | First line 48 (78.7%) Switch 13 (21.3%) | Various | 24 months | NR | Percentage of patients with 24 week confirmed disability improvement | 10.3% | NR | NA |
| | | | Ocrelizumab | First line 48 (78.7%) Switch 13 (21.3%) | Various | 6 months | NR | Percentage of patients with 24 week confirmed disability worsening | 6.7% | NR | NA |
| | | | Ocrelizumab | First line 48 (78.7%) Switch 13 (21.3%) | Various | 12 months | NR | Percentage of patients with 24 week confirmed disability worsening | 20.5% | NR | NA |
| | | | Ocrelizumab | First line 48 (78.7%) Switch 13 (21.3%) | Various | 18 months | NR | Percentage of patients with 24 week confirmed disability worsening | 20.5% | NR | NA |
| | | | Ocrelizumab | First line 48 (78.7%) Switch 13 (21.3%) | Various | 24 months | NR | Percentage of patients with 24 week confirmed disability worsening | 20.5% | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Rojas (2021) [35] | Argentina, Chile, Mexico | NA | Ocrelizumab | First-line, 12 (42%) | Various | >1 year | 29 | EDSS progression, n (%) | 9 (31%) | 0.09 | Baseline vs follow-up |
| Semper e (2020) [44] | Spain | NA | Ocrelizumab | First-line, 19 Switch, 2 | NR | 17 months | 21 | EDSS progression, n (%) | 1 (5%) | NR | NA |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | | | | |
| Magyari (2020) [42] | Denmark | NA | Ocrelizumab | First line, 131 (41 of which were PPMS) Switch | NR | 6-12 months | 383 | EDSS improvement, n (%) | 80 (21%) | NR | NA |
| | | | Ocrelizumab | First line, 131 (41 of which were PPMS) Switch | NR | 6-12 months | 383 | Stable EDSS score, n (%) | 266 (69%) | NR | NA |
| | | | Ocrelizumab | First line, 131 (41 of which were PPMS) Switch | NR | 6-12 months | 383 | EDSS worsening, n (%) | 37 (10%) | NR | NA |
| Pontieri (2022) [33] | Denmark | NA | Ocrelizumab | First line 174 (15.8%) Switch 930 (84.2%) | Various | 6 months | 379 | Percentage of patients with 24 week confirmed disability improvement | 12.1% | NR | NA |
| | | | Ocrelizumab | First line 174 (15.8%) Switch 930 (84.2%) | Various | 12 months | 309 | Percentage of patients with 24 week confirmed disability improvement | 16.1% | NR | NA |
| | | | Ocrelizumab | First line 174 (15.8%) Switch 930 (84.2%) | Various | 18 months | 111 | Percentage of patients with 24 week confirmed | 17.2% | NR | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | disability improvement | | | |
| | | | Ocrelizumab | First line 174 (15.8%) Switch 930 (84.2%) | Various | 24 months | 11 | Percentage of patients with 24 week confirmed disability improvement | 17% | NR | NA |
| | | | Ocrelizumab | First line 174 (15.8%) Switch 930 (84.2%) | Various | 6 months | 426 | Percentage of patients with 24 week confirmed disability worsening | 4.5% | NR | NA |
| | | | Ocrelizumab | First line 174 (15.8%) Switch 930 (84.2%) | Various | 12 months | 343 | Percentage of patients with 24 week confirmed disability worsening | 8.4% | NR | NA |
| | | | Ocrelizumab | First line 174 (15.8%) Switch 930 (84.2%) | Various | 18 months | 124 | Percentage of patients with 24 week confirmed disability worsening | 8.9% | NR | NA |
| | | | Ocrelizumab | First line 174 (15.8%) Switch 930 (84.2%) | Various | 24 months | 12 | Percentage of patients with 24 week confirmed disability worsening | 9% | NR | NA |
| Van Lierop (2021) [49] | Netherlands | NA | Ocrelizumab | First line, 39 (23.6%) Switch, 126 (76.4%) | Various | 45 weeks (median follow-up) | 96 | EDSS progression, n (%) | 23 (24%) | NR | NA |

Abbreviations: CDI, confirmed disability improvement; CDP, confirmed disability progression; CDW, confirmed disability worsening; EDSS, expanded disability status scale; MS, multiple sclerosis; NA, not applicable; NR, not reported

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

## Supplementary Table 10. Studies reporting evidence of disease activity and no evidence of disease activity

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | | | | | |
| Bigaut (2022) [1] | France | NA | Ocrelizumab | Switch | Natalizumab | 1 year | 33 | Number & % of patients with ≥1 criteria of EDA | 5 (15%) | NA | <0.001 | Chi-squared, Ocrelizumab vs fingolimod<br>p value |
| | | | Fingolimod | Switch | Natalizumab | 1 year | 43 | Number & % of patients with ≥1 criteria of EDA | 24 (56%) | NA | <0.001 | Chi-squared, Ocrelizumab vs fingolimod<br>p value |
| Cellerino (2021) [39] | Italy | RRMS | Ocrelizumab | NR | NR | 2 years | 93 | % of patients with NEDA-3 status | 62% | NA | NA | NA |
| | | | | | | 2 years + 100-day re-baseline | 93 | % of patients with NEDA-3 status | 72% | NA | NA | NA |
| | | | | | | 2 years + 180-day re-baseline | 93 | % of patients with NEDA-3 status | 77% | NA | NA | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fernandez-Diaz (2021) [30] | Spain | RRMS | Ocrelizumab | First-line, 36 (25%)<br>Switch, 108 (75%) | Various | Follow up | 44 | Number & % of patients with NEDA-3 | 40 (91%) | NA | NR | NA |
| Garcia-Canibano (2021) [7] | Qatar | NA | Ocrelizumab | First line, 24 (38%)<br>Switch, 36 (62%) | Various | 19.3 months | 57 | Number and % of patients with NEDA | 41 (72%) | NA | NA | NA |
| | | | | | | NA | NR | Estimated median follow-up time with NEDA on ocrelizumab using Kaplan Meier survival analysis | 34 months | 18.5, 49.5 (95% CI) | NA | NA |
| Rolfes (2021) [13] | Germany | Standard interval dosing | Ocrelizumab | First line, 38 (20.1%) Switch, 164 (79.9%) | NR | Baseline | 202 | Number and % of patients with loss of NEDA | 39 (19.3%) | NA | NA | NA |
| | | Extended interval dosing | Ocrelizumab | First line, 24 (21.3%) Switch, 92 (78.7%) | NR | Baseline | 116 | Number and % of patients with loss of NEDA | 17 (14.6%) | NA | NA | NA |
| | | Standard interval dosing | Ocrelizumab | First line, 38 (20.1%) Switch, 164 (79.9%) | NR | Follow-up | 202 | Number and % of patients with loss of NEDA | 39 (19.3%) | NA | NA | NA |

| Author (year) | Country | Subgroup | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Odds ratio for loss of NEDA - extended interval dosing vs standard interval dosing | 1.266 | 0.695-2.305 (95% CI) | 0.441 | NA |
| **Primary progressive MS** | | | | | | | | | | | | |
| Cellerino (2021)[39] | Italy | PPMS | Ocrelizumab | NR | NR | 2 years | 43 | % of patients with NEDA-3 status | 54.6 % | NA | NR | NA |
| | | | | | | 2 years + 100-day re-baseline | 43 | % of patients with NEDA-3 status | 71.4 % | NA | NR | NA |
| | | | | | | 2 years + 180-day re-baseline | 43 | % of patients with NEDA-3 status | 71.9 % | NA | NR | NA |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | | | | | |
| Sempere (2020)[44] | Spain | RMS | Ocrelizumab | First-line & switch | Various | >1 year | 33 | Proportion of patients with NEDA | 31 (94%) | NA | NR | NA |

Abbreviations: EDA, evidence of disease activity; MS, multiple sclerosis; NA, not applicable; NEDA, no evidence of disease activity; NR, not reported

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

## Supplementary Table 11. Studies reporting health-related quality of life

| Author (year) | Country | Intervention | Line of intervention, n (%) | Switched from | Time point | Sample size | Outcome measure | Outcome value | Data spread (SD) | p value | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Relapsing remitting MS** | | | | | | | | | | | |
| Bossart (2022) [2] | Switzerland | Ocrelizumab | NR | NR | 6 months | 98 | MFIS | 30.5 | 21.5 | NA | NA |
| | | Fingolimod | NR | NR | 6 months | 139 | MFIS | 26.4 | 17.7 | | |
| | | Dimethyl fumarate | NR | NR | 6 months | 104 | MFIS | 23.3 | 17.6 | | |
| | | Natalizumab | NR | NR | 6 months | 44 | MFIS | 28.2 | 20.8 | | |
| | | Teriflunomide | NR | NR | 6 months | 31 | MFIS | 28.3 | 21.6 | | |
| | | Ocrelizumab | NR | NR | 6 months | 98 | EQ-5D index | 80.9 | 15.8 | NA | NA |
| | | Fingolimod | NR | NR | 6 months | 139 | EQ-5D index | 83.9 | 14.0 | | |
| | | Dimethyl fumarate | NR | NR | 6 months | 104 | EQ-5D index | 86.6 | 13.8 | | |
| | | Natalizumab | NR | NR | 6 months | 44 | EQ-5D index | 80.2 | 16.2 | | |
| | | Teriflunomide | NR | NR | 6 months | 31 | EQ-5D index | 79.7 | 14.8 | | |
| **Primary progressive MS** | | | | | | | | | | | |
| Impellizzeri (2019) [22] | NR | Ocrelizumab | NR | NR | 12 months | 93 | MSQoL-54 | Stable | NA | NA | NA |
| **Relapsing remitting MS and primary progressive MS combined population[a]** | | | | | | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Smoot (2021)[45] | USA | Ocrelizumab | First-line, 96 (27.4%) | Various | 12 months | 355 | BDI-II (mean difference from baseline) | -0.61 | 7.6 | 0.40 | NA |
| | | | | | | | MFIS (mean change from baseline) | -3.7 | 14.1 | 0.02 | NA |

Abbreviations: BDI-II, Beck Depression Inventory-II; EQ-5D, EuroQol 5 dimension instrument; MFIS, Modified Fatigue Impact Scale; MS, multiple sclerosis; MSQoL-54, Multiple Sclerosis Quality of Life-54 Instrument; NA, not applicable; NR, not reported

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

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