DOI: 10.4274/jmsr.galenos.2025.2025-3-2

J Mult Scler Res

REVIEW

Management of Infusion-related Reactions (IRRs) in Patients Receiving Ocrelizumab for Multiple Sclerosis (MS) Treatment: A Systematic Review

Mohammad Nabeel Baniamer[1], Hasan Ibrahim Matar[1], Basil Nabeel Baniamer[2], Ammar Samer Altaweel[1], Aya Abd-elsalam Al-Rjoub[1], Abdallah Najeh Aletaywi[1], Abdullah I. Alsarayrah[1]

[1]Jordan University of Science and Technology Faculty of Medicine, Ibrid, Jordan
[2]Yarmouk University Faculty of Medicine, Ibrid, Jordan

Abstract

Ocrelizumab demonstrates positive outcomes in patients with multiple sclerosis. However, approximately 40% of patients experience infusion-related reactions (IRRs), which can reduce adherence despite premedications. This review examines the safety of shortened infusion protocols in reducing IRRs and improving the patient experience. Additionally, other strategies for minimizing IRRs are discussed. Scopus, PubMed, and the Cochrane Library were searched up to November 30, 2024, for cohort studies, as well as randomized and non-randomized clinical trials. Seven studies were included following two stages of screening. The primary outcome was a documented reduction in the incidence rate of IRRs. The seven included studies comprised a total of 1,834 patients. Overall, shorter-infusion protocols were found to be safe as conventional protocols, with only a slight increase in IRR incidence. Patients receiving shorter infusions at home reported higher satisfaction, comfort, and confidence. Splitting the first dose appears to be safer than administering a full dose at once, although a single full dose is also relatively safe. Shorter infusion rates and a single full dose of ocrelizumab are generally preferred to save time and effort. Premedication has been shown to reduce IRRs, and patients report greater comfort with at-home infusions. Further clinical trials are needed to evaluate all proposed procedures and to establish a comprehensive understanding of the optimal management strategies for ocrelizumab-related IRRs.

Keywords: Systemic review, multiple sclerosis, ocrelizumab, infusion-related reactions, shorter infusion, management

Introduction

Multiple sclerosis (MS) is a chronic autoimmune disorder of the central nervous system characterized by inflammation, demyelination, and axonal damage (1). This debilitating disease presents with a wide range of symptoms, including sensory disturbances, motor impairments, and cognitive dysfunction. MS disproportionately affects younger adults aged 20-44 years. Globally, it accounted for over 973,300 disability-adjusted life years and 16,300 deaths in 2021, underscoring its substantial impact on health and productivity (2,3).

The advent of disease-modifying therapies has transformed MS management, providing options to reduce relapse rates, slow disease progression, and enhance quality of life. Among these, ocrelizumab—a humanized monoclonal antibody (mAb) targeting CD20-positive B-cells—has demonstrated efficacy in both relapsing and primary progressive forms of MS (4,5). By modulating immune activity, ocrelizumab targets the inflammatory mechanisms driving the disease. Despite its therapeutic benefits, its use can be complicated by infusion-related reactions (IRRs), ranging from mild symptoms, such as itching and flushing, to severe issues like shortness of breath and hypotension (6).

Address for Correspondence: Mohammad Nabeel Baniamer, Jordan University of Science and Technology Faculty of Medicine, Ibrid, Jordan
E-mail: mnbaniamer23@med.just.edu.jo **ORCID-ID:** orcid.org/0009-0005-8326-7994
Received: 28.03.2025 **Accepted:** 29.09.2025 **Epub:** 15.10.2025

Cite this article as: Baniamer MN, Matar HI, Baniamer BN, Altaweel AS, Al-Rjoub AA, Aletaywi AN, Alsarayrah AI. Management of infusion-related reactions (IRRs) in patients receiving ocrelizumab for multiple sclerosis (MS) treatment: a systematic review. J Mult Scler Res. [Epub Ahead of Print]

IRRs, often triggered by cytokine release during infusion, represent a significant barrier to treatment adherence and optimal outcomes. These reactions are commonly observed with mAb treatments and can occur via multiple pathogenic mechanisms, including cytokine release syndrome and hypersensitivity reactions mediated by immunoglobulins E and G (7,8). IRRs may delay therapy, lead to treatment discontinuation, or diminish the therapeutic benefits of ocrelizumab (9). Effective management of IRRs is essential and includes premedication with antihistamines, corticosteroids, and antipyretics, along with close monitoring during and after infusions (10). Despite these premedication strategies, IRRs still occur in 34-40% of patients receiving ocrelizumab, with the highest incidence observed during the first infusion (11). To address these challenges, recent efforts have explored shortening infusion durations as an alternative strategy to reduce IRR incidence and severity while improving overall patient experience.

While existing research has examined IRRs with monoclonal antibodies, there remains a need for more focused investigation of ocrelizumab-specific IRRs. A deeper understanding of their frequency, underlying mechanisms, and risk factors could refine clinical protocols and enhance safety. Clarifying these mechanisms may also improve risk prediction and inform targeted strategies to mitigate adverse reactions.

The absence of well-defined criteria for stratifying patients' IRR risk presents a challenge to personalizing ocrelizumab therapy. In addition, the long-term impact of IRRs on treatment adherence remains understudied; such reactions may lead to therapy discontinuation or hesitation to continue, ultimately compromising effective disease management. By systematically evaluating shortened versus conventional infusion protocols, this review aims to assess whether reduced administration times can lower IRR rates while maintaining treatment efficacy. The findings may inform more patient-centered treatment approaches, optimizing adherence and improving quality of care for individuals with MS.

Materials and Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (12).

Search Strategy, PICO, and Study Eligibility Criteria

Databases, including PubMed, Cochrane Library, and Scopus, were searched till November 30, 2024. The search strategy used was: ("IRR*" or "Infusion-Related Reaction*" or "Infusion Reaction*" or "Infusion Event*" or "Infusion Syndrome*") and ("Multiple Sclerosis" or "MS" or "Disseminated Sclerosis" or "Cerebrospinal Sclerosis" or "Autoimmune Demyelinating Disorder" or "Encephalomyelitis Disseminata") and ("Ocrelizumab" or "Ocrevus").

Additionally, we made subtle modifications to the search strategy for each database to ensure the most comprehensive results.

The study population included adult patients aged 18-65 years with MS receiving ocrelizumab as the primary treatment. Interventions included any procedures and/or medications used to reduce the incidence or severity of IRRs. As a control, we used data from patients who were not exposed to the interventions described above. The primary outcome of interest was the reduction in IRRs, measured using the Common Terminology Criteria for Adverse Events. Secondary outcomes included treatment satisfaction (Treatment Satisfaction Questionnaire for Medication), sleepiness (Stanford Sleepiness Scale), fatigue (Visual Analog Scale-Fatigue; Modified Fatigue Impact Scale), and disease impact (Multiple Sclerosis Impact Scale) scores.

We included prospective and retrospective studies, randomized and non-randomized trials, and sub-studies that assessed ocrelizumab IRR incidence as a primary outcome. Studies evaluating IRR incidence as a secondary outcome were included only if they reported sufficient data. Case reports and case series were excluded, as none provided detailed data or management procedures. We also excluded studies lacking essential data, animal or *in vitro* studies, book chapters, conference abstracts, and publications presented solely as commentaries.

Study Screening, Quality Assessment, and Data Extraction

Initially, one researcher identified and eliminated duplicate studies based on title, author, publication year, and DOI. Screening was then conducted in two stages: in stage 1, studies were evaluated based on titles and abstracts; in stage 2, full-text screening was performed using the aforementioned eligibility criteria. Both stages were performed by three independent authors, with a fourth author resolving any conflict.

Quality assessment was performed using the Cochrane's Risk of Bias Tool for randomized trials. Non-randomized trials were evaluated using the Newcastle-Ottawa Scale (NOS). Assessments were conducted independently by two authors, with a third author resolving any disagreements. Data from eligible studies were extracted using a standardized Excel form, including publication characteristics (authors, national clinical trial numbers, year, study duration) and study design (intervention details, control and treatment groups, total number of participants). Patient demographics (age and gender), as well as study outcomes and conclusions, were also recorded.

Search Results

The literature search identified a total of 745 studies using a pre-formatted search strategy: 59 from PubMed, 645 from Scopus, and 41 from Cochrane. Using EndNote, 76 duplicate studies were removed before the first stage of screening. A total of 699 studies underwent title and abstract screening, of

which 635 were excluded. Following full-text review, seven of the remaining 41 studies met the inclusion criteria and were included in this systematic review.

See PRISMA flow diagram (Figure 1).

Study Characteristics

The seven included studies comprised a total of 1,834 patients. Five studies (9,13-16) were clinical trials: four of which were randomized and one non-randomized. Two (17,18) were cohort studies: one was a single-center cohort (comparative analysis), and the other was an open-label, single-arm, non-randomized study. Study durations ranged from 2 to 252 weeks. All studies reported comparable mean ages, ranging from 34.2 to 48.2 years, and EDSS scores ranging from 0 to 6.5. Sample sizes varied from 19 to 745 participants. Regarding gender distribution, 586 patients were male and 1,248 were female, representing 68% female participants. An analysis of 4,495 MS patients found that 3,030 were female (67.4%), confirming that our study population aligns with the gender-based prevalence of MS (19) (Tables 1 and 2).

Four studies (13-15,18) evaluated the safety of rapid ocrelizumab infusion and its effect on IRRs. One study assessed IRRs and

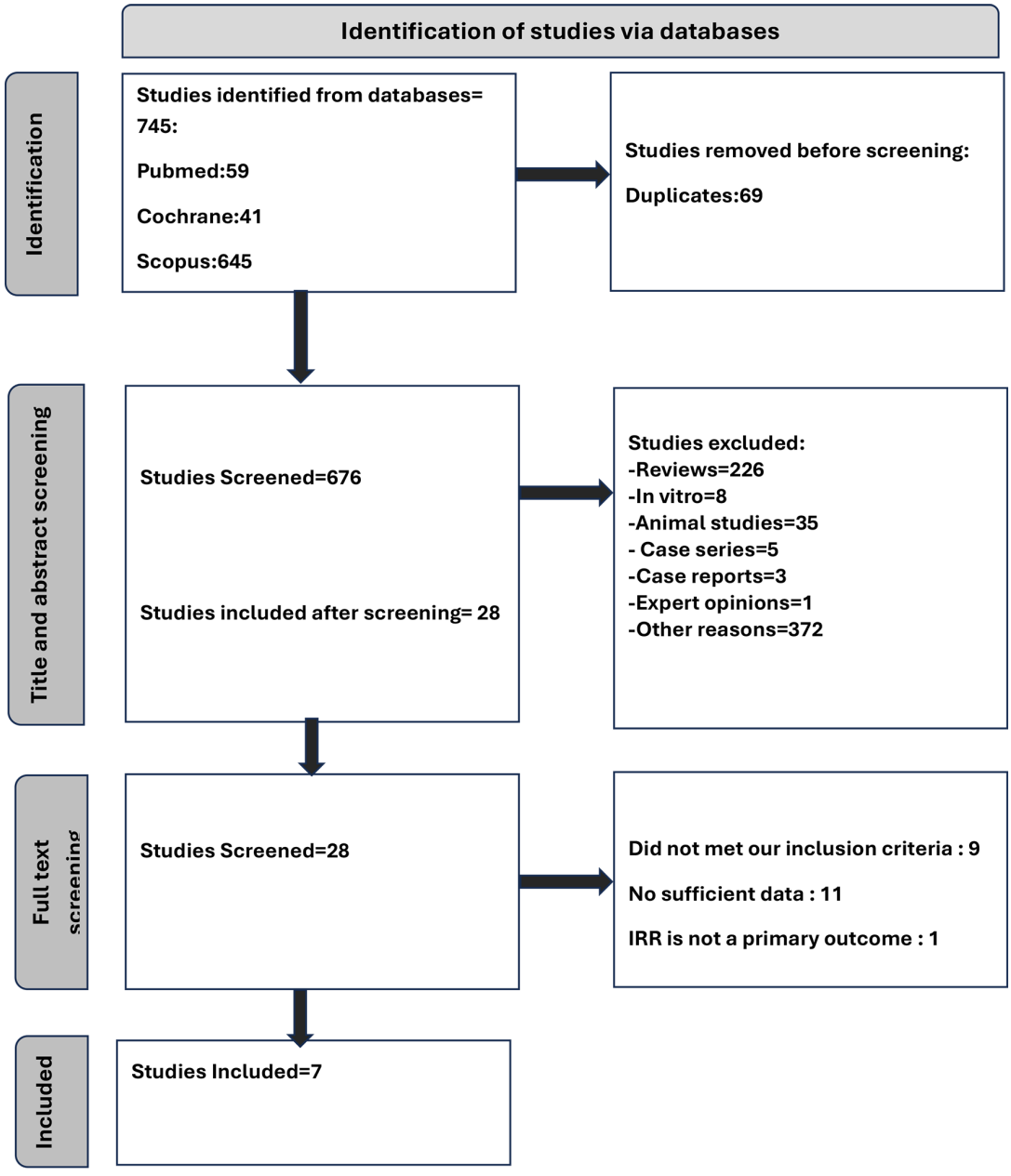

Figure 1. PRISMA flow diagram of study selection. Flow diagram summarizing the identification, screening, eligibility, and inclusion process of studies in the systematic review

PRISMA: Preferred reporting items for systematic reviews and meta-analyses

Table 1. Demographic and clinical characteristics of included studies. Overview of patient demographics and clinical characteristics across the included studies, including treatment regimens, age, gender distribution, and MS subtypes

Study	Treatment regime (n)	Gender male/female	Age, year (mean ± SD)	Type of phenotype (n)	EDSS score (mean ± SD)
1. Zanetta et al. (18)	**OCR-RI, OCR-SI**	**154/215**	**39.9 (10.5)**	**PPMS =75 RRMS =274 SPMS =20**	**3 (3.33)**
2. Abbasi Kasbi et al. (16)	**Ocrelizumab**	**82/250**	**38 (9.9)**	**PPMS RRMS Total: 332**	**3 (2.22)**
3. Vollmer et al. (13)	**OCR-SI**	**Cohort 1: 36/59 Cohort 2: 12/34 Total: 48/93**	**Cohort 1: 41.7 (8.8) Cohort 2: 41.1 (8.7) Total: 41.5(8.8)**	**PPMS =12 RMS =129**	**2.64 (1.67)**
4. Smoot et al. (9)	**Ocrelizumab pretreated with cetirizine, ocrelizumab pretreated with diphenhydramine**	**Cetirizine: 1/6 Diphenhydramine: 3/9 Total: 4/15**	**Cetirizine: 48.2 (4) Diphenhydramine: 46.3 (3.1) Total: 47.5 (3.6)**	**PPMS =1 RRMS =16 SPMS =2**	**Not mentioned**
5. Hartung et al. (14)	**OCR-RI, OCR-SI**	**271/474**	**34.2(8.8)**	**PPMS RRMS**	**Not mentioned**
6. Bermel et al. (15) NCT0237856	OCR-SI	**Not mentioned**	**36.7 (8.1)**	**PPMS RMS**	**Not mentioned**
7. Barrera et al. (17) NCT04650321	Home-based ocrelizumab	27/72	42.3 (7.7)	PPMS =13 RMS =178	2 (1.11)

MS: Multiple sclerosis, SD: Standard deviation, EDSS: Expanded Disability Status Scale, OCR-RI: Ocrelizumab rapid infusion, OCR-SI: Ocrelizumab standard infusion, PPMS: Primary progressive multiple sclerosis, RRMS: Relapsing remitting multiple sclerosis

Table 2. Summary of study characteristics. Overview of study designs, participant numbers, treatment arms, and study durations for the seven studies included in the review

Study	Type of ocrelizumab	Treatment group (number of participants)	Total number of participants (n)	Study period (weeks)
1. Zanetta et al. (18)	**OCR-RI OCR-SI**	**OCR-RI: 283 OCR-SI: 86**	**369**	**291**
2. Abbasi Kasbi et al. (16)	**Two 300 mg ocrelizumab doses/ One 600 mg ocrelizumab dose**	**Two 300 mg ocrelizumab doses: 150 One 600 mg ocrelizumab dose: 182**	**332**	**Not mentioned**
3. Vollmer et al. (13)	**OCR-SI**	**Cohort 1: 95 Cohort 2: 46**	**141**	**48**
4. Smoot et al. (9)	**Ocrelizumab pretreated with cetirizine/ Ocrelizumab pretreated with diphenhydramine**	**Ocrelizumab pretreated with cetirizine: 10/ Ocrelizumab pretreated with diphenhydramine: 9**	**19**	**24**
5. Hartung et al. (14)	**OCR-RI OCR-SI**	**OCR-RI: 373 OCR-SI: 372**	**745**	**120**
6. Bermel et al. (15) NCT0237856	**OCR-SI**	**OCR-SI: 129**	**129**	**96**
7. Barrera et al. (17) NCT04650321	**Home-based ocrelizumab**	**Home-based ocrelizumab: 99**	**99**	**2**

OCR-RI: Ocrelizumab rapid infusion, OCR-SI: Ocrelizumab standard infusion

patient satisfaction using patient-reported outcomes during at-home ocrelizumab administration (17). Another study examined the effects of administering 600 mg of ocrelizumab and compared it with the current standard protocol in terms of IRR frequency during the first infusion (16). The final study focused on optimizing treatment safety by investigating diphenhydramine as a premedication and its impact on reaction severity and patient satisfaction (9). All studies included both types of MS, except for two that enrolled only patients with relapsing-remitting MS (14,17).

Risk of Bias

Due to the heterogeneity of study designs, the risk of bias for included studies was assessed using two tools: the NOS (20) for four non-randomized studies (13,15,17,18), and the risk of bias tool (ROB) (21) for three randomized studies (9,14,16). All studies evaluated with NOS scored between 7-8 (Figure 2), indicating a low ROB. Using ROB, one study was assessed (9) as having a high risk of bias due to concerns about outcome measurement and selective reporting. Another study was rated as having some concerns regarding the randomization process and a high ROB for outcome measurement (16). The final study was judged to have a low ROB score (Figure 3) (14).

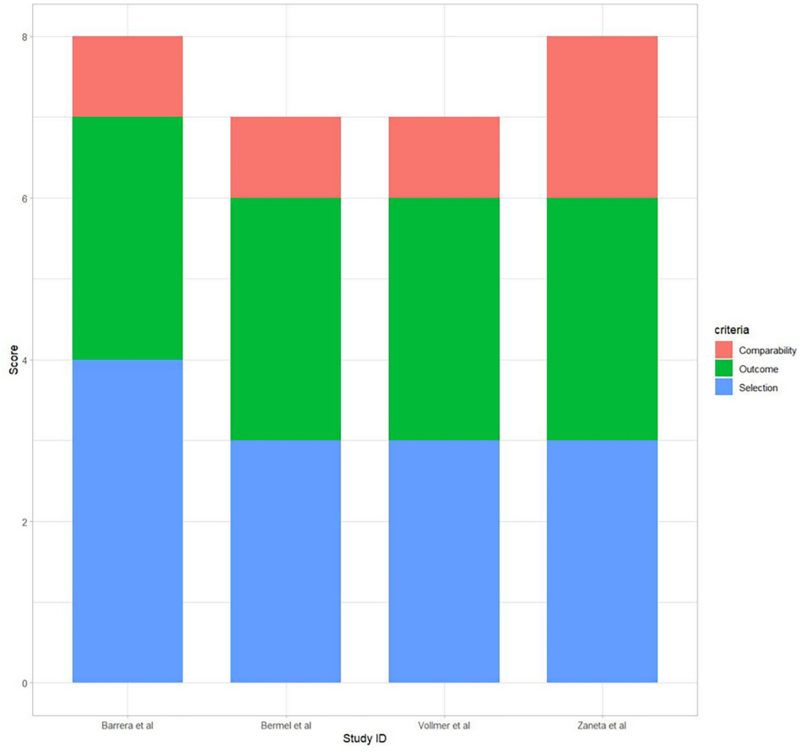

Figure 2. Newcastle-Ottawa Scale (NOS) assessment for non-randomized studies. Quality assessment scores of the included non-randomized studies based on the NOS criteria

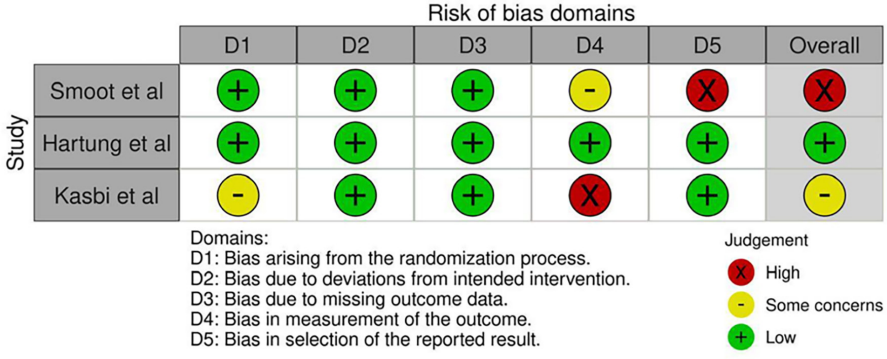

Figure 3. Risk of bias by domain for randomized studies. Domain-specific risk of bias assessments for randomized trials, evaluated using the ROB2 tool and categorized by level of concern

ROB2: Cochrane's Risk of Bias Tool

Outcomes

Conventional vs. Shorter Infusion

One sub-study, comparing conventional and shorter infusion groups in patients receiving six doses of ocrelizumab 600 mg, found a similar number of patients experiencing IRRs after the first dose (101/373 vs. 107/372 patients, respectively) (14). Across all six doses in the sub-study, the proportion of patients experiencing IRRs was similar between groups (41.6% vs. 46.2%). Most IRRs were mild or moderate (Grade 1-2), occurring in 99.4% of patients in the conventional infusion group and 97.7% in the shorter infusion group. Only five reactions were severe (Grade 3): one in the conventional infusion group and four in the shorter infusion group.

No Grade 3 or higher IRRs were reported after the second dose, and no patients discontinued treatment due to IRRs. The most common IRRs during the first infusion were throat irritation (18.8% vs. 29.9%) and dysphagia (6.9% vs. 7.5%) in the conventional and shorter infusion groups, respectively. Within 24 hours post-infusion, headache (25.7% vs. 17.8%) and fatigue (22.8% vs. 18.7%) were the most frequently reported adverse events.

In another sub-study (15), patients receiving a single dose of ocrelizumab (600 mg) via shorter infusion experienced no severe or life-threatening IRRs. Grade 1-2 IRRs were reported in 12.4% of patients, consistent with findings from the main study, particularly at dose 3. Infusion rate reduction or treatment interruption was required for nine patients, as observed at dose 3, and all IRRs resolved without further medical intervention.

In study, patients receiving a single dose of home-based ocrelizumab (600 mg) infusion over 2 h were assessed, with 25.3% (95% CI: 16.7-33.8%) experiencing an IRR of any grade (17). Of these, 18.2% were Grade 1 and 7.1% were Grade 2, with no IRRs ≥ Grade 3 reported.

Another study evaluated patients receiving varying numbers of ocrelizumab 600 mg doses with an infusion time reduced from 3.5 to 2 h (18). Overall, 25 patients (8.8%) in the rapid infusion group and 13 patients (15.1%) in the conventional group experienced IRRs. The frequency of IRRs did not differ significantly between the two groups. Most IRRs were mild (Grade 1, 81.6%) or moderate (Grade 2, 18.4%).

Full First Dose (600 mg) vs. Split Dose (300 mg)

One study compared IRRs of the first dose 600 mg vs. two 300 mg showed that most of the IRRs were mild in both (two 300 mg doses and one 600 mg dose) groups (16).

Shorter Full Dose vs. Shorter Split Dose

In sub-study, patients were divided into two cohorts: cohort 1 (n=95) received 600 mg of ocrelizumab over 2 hours, while cohort 2 (n=46) received a split dose of 300 mg over 1.5 hours (13). The results were as follows:

In cohort 1, 35 patients experienced IRRs during the first dose and 30 during the second dose, whereas only 7 patients in cohort 2 experienced IRRs. No observed Grade 3 or 4 IRRs were reported in either cohort.

In cohort 1, 14% of patients experienced IRRs that required interruption or slowing of the infusion, while no such interruptions occurred in cohort 2.

Premedication

IRRs were compared between groups that received different premedications in the study (9): one group received oral cetirizine (10 mg), and the other received diphenhydramine (25 mg). Following the first infusion of the initial dose, each group reported six IRRs (corresponding to 60% of the cetirizine group and 67% of the diphenhydramine group). At the end of the study (after two doses), 80% of patients in the cetirizine group and 89% in the diphenhydramine group experienced at least one IRR. The incidence of IRRs was similar between groups, with no increase in severity and no Grade 3 events reported (Table 3).

Patient Satisfaction

After blinding in the study, most patients in the conventional group chose to switch to short-infusion (79.7% (n=279/350), whereas most patients in the short-infusion group opted to continue with short-infusions (94.6%; n=331/350) (14). Among patients who preferred conventional infusions (n=90), 57.7% (n=51/90) had experienced IRRs, compared to 42.0% (n=256/610) of those who preferred shorter infusions.

A significant improvement in the overall infusion experience was reported by patients receiving at-home infusions (17). They described feeling more comfortable, safer, and respected. They also noted that nurses provided clearer explanations compared with the hospitals.

Discussion

This systematic review provides the most recent data about the procedural interventions to reduce IRRs in patients receiving ocrelizumab for MS. Management of IRRs is rarely discussed in general, and specifically for ocrelizumab. In patients with MS, experiencing IRRs is critical as it may lead to treatment delays or discontinuation; therefore, preventing these reactions is essential for successful treatment.

"Do no harm" is a fundamental principle in medical practice. Despite this, fewer than 10% of systematically published reviews each year assessed harm associated with medical interventions as their primary objective (22).

Short vs. Conventional

Shorter infusions did not significantly increase the incidence or severity of IRRs in any of the studies (2-6). However, in one study, only 0.53% of patients could not tolerate the short infusion and

Table 3. Summary of Interventions and IRR Outcomes. Comparative overview of intervention strategies, infusion-related reaction (IRR) rates, and key findings across the included studies evaluating ocrelizumab administration in patients with multiple sclerosis

Study	Design	Intervention	Comparator	IRR rate	IRR severity	Key finding
Zanetta et al. (18)	Cohort	600 mg over 2 h (Shortened)	600 mg over 3.5 h (Conventional)	8.8% vs. 15.1%	Mild-moderate	Shortened infusion showed fewer IRRs
Abbasi Kasbi et al. (16)	RCT	One 600 mg dose	Two 300 mg doses	Similar	Mostly mild	Both dosing strategies are safe
Vollmer et al. (13)	Open-label phase IIIb	600 mg (2 h) or 300 mg (1.5 h)	None	Cohort 2 had fewer IRRs	No Grade ≥3	Shorter infusions well-tolerated
Smoot et al. (9)	RCT	Cetirizine premedication	Diphenhydramine premedication	80% vs. 89%	No Grade 3	Both premedications are similarly effective
Hartung et al. (14)	RCT	600 mg over 2 h	600 mg over 3.5 h	41.6% vs. 46.2%	Mild-moderate	No significant difference in IRRs
Bermel et al. (15)	Single-arm phase IIIb	600 mg over 2 h	None	12.4%	Grade 1-2 only	No severe IRRs, consistent with prior data
Barrera et al. (17)	Open-label phase IIIb	600 mg at home (2 h)	Historical control	25.3%	Grade 1-2 only	At-home infusion is safe and well-tolerated

IRR: Infusion-related reaction, RCT: Randomized controlled trial

continued ocrelizumab treatment, representing a very small percentage (14).

Short infusion is a feasible and patient-preferred option, with 80% of patients opting to switch to shorter infusions (14). Reducing infusion time also helps optimize clinic scheduling and reduce staff workload. Additionally, at-home short infusions demonstrated positive outcomes and increased patient comfort, providing an alternative for stable MS patients (17).

This is primarily because peak ocrelizumab concentrations were similar between shorter and conventional infusions, suggesting no increase in drug exposure-related toxicity (14). Additionally, premeditation reduced cytokine release and hypersensitivity reactions.

The incidence of IRRs varies widely across studies due to multiple factors. Higher IRR rates in open-label studies suggest ascertainment bias, where clinicians and patients may over-report mild symptoms due to heightened awareness (13). Some studies included treatment-naïve patients (9), who typically experience higher IRR rates compared with pre-exposed patients (18). Additionally, some studies captured IRRs only during infusion (13), while others included events occurring within 24 hours post-infusion (14). Non-standardized IRR definitions across all studies further contribute to variability in reported rates.

Premedication

Methylprednisolone and antihistamines were administered universally (9). Cetirizine was non-inferiority to diphenhydramine in preventing IRRs and was associated with fewer sedative side effects. Some studies allowed on-demand dose adjustments, which may also contribute to variability in reported IRR severity (9).

The First Dose

As per the standard protocol, the first dose is administered in two infusions to reduce IRR rates. However, a single 600 mg dose may be considered, as there is no difference in 24-hour post-infusion or life-threatening reactions. Slightly higher IRR rates can be managed by increasing premedication or reducing the infusion rate (16).

Study Limitations

The included studies were highly heterogeneous, which influenced the reported incidence of IRRs and prevented a meta-analysis. Additionally, long-term safety data were lacking, limiting the generalizability of our findings for long-term management and hindering the detection of complications that may develop over time, such as malignancies and infections. The primary progressive multiple sclerosis cohorts were small compared to the relapsing-remitting multiple sclerosis cohorts. Additionally, only a few studies reported details on premedication administered before infusion.

Future Directions

Further studies are needed to investigate different strategies for reducing IRRs and to establish a safer infusion protocol for ocrelizumab. In particular, additional trials on premedication strategies would significantly contribute to the literature. Long-

term observational studies are also warranted to provide a deeper understanding of ocrelizumab adverse events. Finally, standardizing the definition of IRRs would allow for more consistent and comparable results across studies.

Conclusion

Short and at-home infusions demonstrated safety comparable to conventional infusions, while offering a more comfortable, patient-preferred option. The single 600 mg first infusion was associated with slightly higher IRR rates, which can be easily managed. Both cetirizine and diphenhydramine were effective as premedications, showing similar reductions in IRR incidence.

Footnotes

Authorship Contributions

Concept: M.N.B., H.I.M., Design: M.N.B., B.N.B., A.S.A., Data Collection or Processing: M.N.B., B.N.B., A.S.A., A.A.A.R., A.N.A., A.I.A., Analysis or Interpretation: M.N.B., H.I.M., Literature Search: M.N.B., H.I.M., B.N.B., Writing: M.N.B., H.I.M., B.N.B., A.S.A., A.A.A.R., A.N.A., A.I.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Brück W. The pathology of multiple sclerosis is the result of focal inflammatory demyelination with axonal damage. J Neurol. 2005;252 Suppl 5:v3-9.
2. Wang L, Zhou Y, Song E, Liang J, Pan S, Miao X, Xiao Z. Global, regional, and national burden, trends, and cross-country inequalities of multiple sclerosis from 1990 to 2021, with projections to 2040: a systematic analysis for the Global Burden of Disease Study 2021. Soc Sci Res Netw. 2024. Posted: 15 Oct 2024.
3. Multiple Sclerosis International Federation. Atlas of MS. 3rd ed. London: MSIF; 2020.
4. Filippi M, Amato MP, Centonze D, Gallo P, Gasperini C, Inglese M, Patti F, Pozzilli C, Preziosa P, Trojano M. Early use of high-efficacy disease-modifying therapies makes the difference in people with multiple sclerosis: an expert opinion. J Neurol. 2022;269:5382-5394.
5. Carlson AK, Amin M, Cohen JA. Drugs targeting CD20 in multiple sclerosis: pharmacology, efficacy, safety, and tolerability. Drugs. 2024;84:285-304.
6. Hartung HP; ENSEMBLE Steering Committee members and study investigators. Ocrelizumab shorter infusion: primary results from the ENSEMBLE PLUS substudy in patients with MS. Neurol Neuroimmunol Neuroinflamm. 2020;7:e807.
7. Maggi E, Vultaggio A, Matucci A. Acute infusion reactions induced by monoclonal antibody therapy. Expert Rev Clin Immunol. 2011;7:55-63.
8. Picard M, Galvão VR. Current knowledge and management of hypersensitivity reactions to monoclonal antibodies. J Allergy Clin Immunol Pract. 2017;5:600-609.
9. Smoot K, Marginean H, Gervasi-Follmar T, Chen C. Comparing the risk of infusion-related reactions and tolerability in patients given cetirizine or diphenhydramine prior to ocrelizumab infusion (PRECEPT). Medicina (Kaunas). 2024;60:659.
10. Cáceres MC, Guerrero-Martín J, Pérez-Civantos D, Palomo-López P, Delgado-Mingorance JI, Durán-Gómez N. The importance of early identification of infusion-related reactions to monoclonal antibodies. Ther Clin Risk Manag. 2019;15:965-977.
11. Mayer L, Kappos L, Racke MK, Rammohan K, Traboulsee A, Hauser SL, Julian L, Köndgen H, Li C, Napieralski J, Zheng H, Wolinsky JS. Ocrelizumab infusion experience in patients with relapsing and primary progressive multiple sclerosis: results from the phase 3 randomized OPERA I, OPERA II, and ORATORIO studies. Mult Scler Relat Disord. 2019;30:236-243.
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
13. Vollmer TL, Cohen JA, Alvarez E, Nair KV, Boster A, Katz J, Pardo G, Pei J, Raut P, Merchant S, MacLean E, Pradhan A, Moss B. Safety results of administering ocrelizumab per a shorter infusion protocol in patients with primary progressive and relapsing multiple sclerosis. Mult Scler Relat Disord. 2020;46:102454.
14. Hartung HP, Berger T, Bermel RA, Brochet B, Carroll WM, Holmøy T, Karabudak R, Killestein J, Nos C, Patti F, Perrin Ross A, Vanopdenbosch L, Vollmer T, Buffels R, Garas M, Kadner K, Manfrini M, Wang Q, Freedman MS. ENSEMBLE PLUS: final results of shorter ocrelizumab infusion from a randomized controlled trial. J Neurol. 2024;271:4348-4360.
15. Bermel RA, Waubant E, Pardo G, Bass A, Repovic P, Newsome S, Lindsey JW, Kile D, Pradhan A, Musch B, Zabeti A. Safety evaluation of shorter infusion for ocrelizumab in a substudy of the Phase IIIb CHORDS trial. Ann Clin Transl Neurol. 2021;8:711-715.
16. Abbasi Kasbi N, Ghadiri F, Sahraian MA, Nahayati MA, Moghadasi AN, Langroodi HG, Poursadeghfard M, Hosseini S, Heidari H, Baghbanian SM, Kamali H, Ameli Z, Shahmohammadi S, Navardi S. Comparing infusion-related reactions of the first full dose (600 mg) biosimilar ocrelizumab administration with the standard divided protocol in multiple sclerosis patients: a randomized controlled trial study. Acta Neurol Belg. 2024;124:205-212.
17. Barrera B, Simpson H, Engebretson E, Sillau S, Valdez B, Parra-González J, Winger RC, Epperson LA, Banks A, Pierce K, Spotts M, O'Gean K, Alvarez E, Gross R, Piquet AL, Schreiner T, Corboy JR, Pei J, Vollmer TL, Nair KV. Safety and patient experience with at-home infusion of ocrelizumab for multiple sclerosis. Ann Clin Transl Neurol. 2023;10:579-588.
18. Zanetta C, Faustino P, Guerrieri S, Nozzolillo A, Genchi A, Bucca C, Rocca MA, Moiola L, Filippi M. Fast but not furious: rapid ocrelizumab infusion as a strategy to optimize multiple sclerosis patients' management. J Neurol Sci. 2024;457:122897.
19. Leray E, Moreau T, Fromont A, Edan G. Epidemiology of multiple sclerosis. Rev Neurol (Paris). 2016;172:3-13.
20. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2000. Available from: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
21. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
22. Zorzela L, Golder S, Liu Y, Pilkington K, Hartling L, Joffe A, Loke Y, Vohra S. Quality of reporting in systematic reviews of adverse events: systematic review. BMJ. 2014;348:f7668.