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Site-Specific Treatment and Remission Patterns in Multisite Mucous Membrane Pemphigoid

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IMPORTANCE Mucous membrane pemphigoid (MMP) is a chronic autoimmune blistering disease associated with progressive mucosal scarring and substantial morbidity. Prior studies have often reported remission rates in cohorts combining localized and multisite disease, with limited data on simultaneous remission across all involved sites in patients with multisite disease.

OBJECTIVE To evaluate multisite complete remission (mCR) and site-specific treatment response patterns in patients with multisite MMP.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study took place at a single tertiary dermatology and ophthalmology referral center at the University of Texas Southwestern Medical Center between January 1, 2013, and January 1, 2025. Patients with MMP confirmed by immunopathology, disease involving 2 or more anatomic sites, and 12 months posttreatment follow-up were included.

MAIN OUTCOMES AND MEASURES The primary outcome was mCR, defined as concurrent complete remission across all involved sites regardless of therapy. Secondary outcomes included site-specific remission and relapse patterns, time to remission, and treatment-associated adverse events.

RESULTS Among 77 patients (55 [71%] female; median [IQR] age at diagnosis, 66 [59-72] years), 68 (88%) had high-risk disease involving ocular, laryngeal, esophageal, or anogenital sites. Oral disease was most common, present in 73 patients (95%), followed by ocular disease in 51 (66%) and nasal disease in 38 (49%). Thirty-five patients (45%) achieved mCR in a median (IQR) of 32.0 (20.7-55.3) months. Although all patients demonstrated improvement and 64 (83%) achieved CR at 1 or more sites, persistent oral and ocular diseases frequently prevented mCR. Relapses following site-level CR occurred in 28 of the 64 patients (44%), most frequently at the oral (18 of 28 patients [64%]) and ocular mucosa (14 of 28 patients [50%]); some patients experienced relapse at multiple sites. Rituximab-based regimens and Janus kinase inhibitor therapy were associated with high rates of improvement. Serious adverse events occurred most frequently with cyclophosphamide monotherapy and Janus kinase inhibitor therapy.

CONCLUSIONS AND RELEVANCE In this cohort study, fewer than half of patients with multisite MMP achieved simultaneous multisite remission despite high rates of site-level response. Persistent oral and ocular diseases disproportionately limited global disease control, supporting a site-specific model of disease behavior and highlighting the need for standardized multisite remission outcomes in future studies.

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Supplemental content

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Mucous membrane pemphigoid (MMP) is a chronic autoimmune blistering disease affecting predominantly mucosal surfaces and carries a substantial risk of irreversible scarring causing blindness, airway obstruction, esophageal stricture, and other functional impairment.[1,2] Annual incidence estimates range from 0.87 per million individuals for MMP overall[3] to 1.4 per 100 000 individuals for ocular MMP,[4] with approximately half of patients developing multisite disease.[1,5,6]

International Blistering Disease Consensus Group (IBDCG) recommendations support systemic corticosteroids with steroid-sparing immunosuppressive therapy for initial control of high-risk disease.[7] Treatment is frequently escalated from conventional agents such as dapsone and mycophenolate mofetil[8,9] to rituximab-based regimens,[10,11] intravenous immunoglobin,[12] cyclophosphamide,[13] or Janus kinase inhibitors (JAKi), particularly for ocular disease.[14]

Except for rare exceptions,[13] most MMP studies report remission rates from cohorts including both localized and multisite disease, and define remission by best response at individual sites rather than coordinated remission across all involved sites.[10-21] In this study, we aimed to characterize multisite complete remission (mCR) and site-specific remission patterns in a longitudinal cohort of patients with multisite MMP.

Key Points

Question How often do patients with multisite mucous membrane pemphigoid (MMP) achieve simultaneous remission across all involved sites, and what are the response patterns?

Findings In this cohort study of 77 patients with multisite MMP, 45% achieved simultaneous multisite complete remission (mCR) despite universal improvement, and 83% achieved complete remission at 1 or more sites. Persistent oral and ocular diseases were the most common barriers to mCR, and rituximab-based regimens were associated with lower mCR rates than previously published MMP cohorts.

Meaning In this study, multisite MMP behaved as a site-dependent disease in which persistent activity at oral and ocular surfaces may prevent mCR despite otherwise favorable treatment response.

Methods

We conducted a retrospective cohort study of consecutive patients with MMP evaluated at the University of Texas Southwestern Medical Center, a tertiary referral center, between January 1, 2013, and January 1, 2025, using electronic medical records. Eligible patients had MMP confirmed by direct immunofluorescence or serologic studies, involvement of 2 or more anatomic sites, and 12 months or longer of posttreatment follow-up (eFigure 1 in Supplement 1). All were evaluated by a board-certified dermatologist (A.R.D.) specializing in immunobullous disease. Ocular disease activity was graded using a standardized approach[22] by a board-certified ophthalmologist (J.H.C.) trained in cicatrizing conjunctivitis. Twenty-seven patients overlapped with prior institutional cohorts; however, those studies included both localized ocular MMP and multisite MMP with ocular involvement.[14,23,24] This study was approved by the institutional review board of the University of Texas Southwestern Medical Center with a waiver of informed consent owing to the retrospective nature of the study. We followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

The primary outcome was mCR, defined as concurrent complete remission across all involved sites regardless of ongoing therapy. Site-level response was categorized as CR, partial response, or no response using IBDCG definitions[7,25] (eTable 1 in Supplement 1). Improvement was defined as CR or partial response. Secondary outcomes included steroid-free remission, durable drug-free remission, mCR on minimal therapy, time to first site-level CR, and relapse after CR (eTable 1 in Supplement 1).

High-risk sites included ocular, laryngeal, esophageal, and/or anogenital involvement, while cutaneous and oral diseases were low risk.[7] Treatment response was analyzed at the patient-drug level. Time-to-event outcomes were summarized using medians and IQRs; time to first CR was visualized using Kaplan-Meier methods and compared using a marginal Cox proportional hazards model with patient-level robust sandwich variance. Pairwise site-association analyses and standard comparative testing are detailed in the eMethods in Supplement 1. Analyses used complete-case data, with 2-sided $P < .05$ considered statistically significant. All statistical analyses were performed using R, version 4.6.1 (R Foundation for Statistical Computing).

Results

Seventy-seven patients met inclusion criteria (eFigure 1 in Supplement 1). Of these patients, 55 (71%) were female, the median (IQR) age at diagnosis was 66 (59-72) years, and 68 (88%) had high-risk disease. Aside from longer follow-up in the cohort with high-risk disease vs with non-high-risk disease (median [IQR], 55 [22-88] months vs 18 [16-28] months; $P = .01$), baseline characteristics were similar between severity groups (**Table 1**).

Oral involvement was most common, present in 73 patients (95%), followed by ocular disease in 51 (66%) and nasal disease in 38 (49%) (**Table 2**). Patients had a median (IQR) of 3 (2-4) involved sites, and 55 (71%) had 3 or more sites involved. Oral and ocular diseases were the most common initial presentations, occurring in 37 patients (48%) and 22 patients (29%), respectively. No statistically significant baseline site coinvolvement was identified.

Thirty-five patients (45%) achieved mCR after a median (IQR) of 32.0 (20.7-55.3) months, with 13 (37%) maintaining mCR on minimal therapy[25] (Table 1). Patients with non-high-risk disease reached mCR sooner than patients with high-risk disease (median [IQR], 17.9 [14.8-19.9] months vs 37.7 [23.9-56.7] months; $P < .001$). All 77 patients improved, and 64 (83%) achieved CR at 1 or more sites, whereas durable drug-free remission was uncommon, occurring in 7 patients (9%), but more

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Table 1. Baseline Characteristics, Immunopathologic Features, and Clinical Outcomes of Patients With Multisite Mucous Membrane Pemphigoid (MMP), Stratified by High-Risk Disease Status

Characteristic	No./total No. (%)		
	Overall cohort (N = 77)	Non-high-risk disease cohort (n = 9)	High-risk disease cohort (n = 68)[a]
Age at diagnosis, median (IQR), y	66 (59-72)	58 (54-66)	66 (59-73)
Sex[b]			
Female	55/77 (71)	6/9 (67)	49/68 (72)
Male	22/77 (29)	3/9 (33)	17/68 (25)
Race and ethnicity[b]			
Latin American	6/77 (8)	0	6/68 (9)
Non–Latin American or declined	71/77 (92)	9/9 (100)	62/68 (91)
White	69/77 (90)	8/9 (89)	61/68 (90)
Other race[c]	8/77 (10)	1/9 (11)	7/68 (10)
Follow-up duration, median (IQR), mo	52 (22-88)	18 (16-28)[d]	55 (24-93)[d]
Charlson Comorbidity Index, median (IQR)	1 (0-2)	1 (0-2)	1 (0-2)
Noncutaneous malignant neoplasm			
Lifetime malignant neoplasm[e]	19/77 (25)	2/9 (22)	17/68 (25)
Before MMP treatment initiation	13/19 (68)	1/2 (50)	12/17 (71)
During or after MMP treatment initiation[f]	6/19 (32)	1/2 (17)	5/17 (29)
DIF biopsy findings			
DIF consistent with MMP (any positive)	74/77 (96)	9/9 (100)	65/68 (96)
IgG deposition at BMZ	73/77 (95)	9/9 (100)	64/68 (94)
IgA deposition at BMZ	27/77 (35)	2/9 (22)	25/68 (37)
IgG and IgA deposition at BMZ	27/77 (35)	1/9 (11)	26/68 (38)
C3 deposition at BMZ	43/77 (56)	8/9 (89)	35/68 (51)
IIF biopsy findings			
IIF consistent with MMP (any positive)	22/66 (33)	2/9 (22)	20/57 (35)
IIF IgG roof	12/66 (18)	2/9 (22)	10/57 (18)
IIF IgA roof	8/66 (12)	1/9 (11)	7/57 (12)
IIF IgG floor	3/66 (5)	0	3/57 (5)
IIF IgA floor	0	0	0
IIF IgG + IgA (roof or floor)	2/66 (3)	1/9 (11)	1/57 (2)
IIF any IgG (roof or floor)	15/66 (23)	2/9 (22)	13/57 (23)
IIF any IgA (roof or floor)	8/66 (12)	1/9 (11)	7/57 (12)
ELISA serologic findings			
Anti-BP180 positive	23/54 (43)	3/8 (38)	20/46 (43)
Anti-BP230 positive	10/54 (19)	0	10/46 (22)
DIF + IIF composite findings			
Any IgG positive	75/77 (97)	9/9 (100)	66/68 (97)
Any IgA positive	30/77 (39)	1/9 (11)	29/68 (43)
mCR[g]			
Patients with mCR[h]	35/77 (45)	4/9 (44)	31/68 (46)
Time to mCR, median (IQR), mo	32.0 (20.7-55.3)	17.9 (14.8-19.9)[d]	37.7 (23.9-56.6)[d]
mCR on minimal therapy[i]	13/35 (37)	3/4 (75)	10/31 (32)
mCR on ongoing biologic therapy[i]	19/35 (54)	0	19/31 (61)
Secondary remission outcomes			
Patients with steroid-free remission	34/77 (44)	4/9 (44)	30/68 (44)
Time to steroid-free remission, median (IQR), mo	34.5 (21.5-55.5)	17.9 (14.8-19.9)	38.1(24.7-57.0)
Patients with durable drug-free remission[j]	7/77 (9)	2/9 (22)[k]	5/68 (7)[k]
Time to durable drug-free remission, median (IQR), mo	44.6 (33.0-57.0)	81.0 (52.0-110.0)	37.5 (29.5-44.5)

Abbreviations: BMZ, basement membrane zone; DIF, direct immunofluorescence; ELISA, enzyme-linked immunosorbent assay; IIF, indirect immunofluorescence; mCR, multisite complete remission.

[a] High-risk disease was defined as involvement of ocular, laryngeal, esophageal, or anogenital sites.[7]

[b] Patient sex, race, and ethnicity were self-reported by the patient in the electronic medical record.

[c] The other race category includes patients who self-reported as Asian or Black or who declined to report. These groups were reported together owing to small sample sizes.

[d] Statistically significant (P = .01; Mann-Whitney U test).

[e] Malignant neoplasms included breast adenocarcinoma (n = 8), prostate carcinoma (n = 5), papillary thyroid carcinoma (n = 3), colon adenocarcinoma (n = 2), ovarian epithelial carcinoma (n = 1), pancreatic adenocarcinoma (n = 1), and renal cell carcinoma (n = 1).

[f] Two patients developed 2 simultaneous unrelated cancers and were counted once.

[g] Patients' best response was considered for each outcome.

[h] Three patients reached mCR on mycophenolate mofetil, 1500 mg, twice daily and thus did not meet criteria for minimal therapy or biologic therapy.

[i] As defined by the International Blistering Disease Consensus Group.[25]

[j] No difference was seen between patients who reached mCR off therapy, defined by the International Blistering Disease Consensus Group as no therapy for 2 months,[25] and durable drug free remission, defined as no therapy for 6 months.

[k] Statistically significant (P = .05; Fisher exact test).

frequent in patients with non-high-risk disease (2 of 9 [22%] vs 5 of 68 [7%]; P = .05) (Table 1).

Site-level CR ranged from 89% for cutaneous disease (24 of 27 patients) to 42% for esophageal disease (5 of 12 patients) (Table 2). There was a statistically significant difference between time-to-first CR between sites (robust Wald χ^2_6 = 29.9; P < .001; eFigure 2 in Supplement 1). In pairwise comparisons from the marginal Cox model, patients with

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Table 2. Site-Specific Disease Involvement, Treatment Response, and Relapse Patterns Among Patients With Multisite Mucous Membrane Pemphigoid

Outcome	Site, No./total No. (%)						
	Ocular	Oral	Nasal	Cutaneous	Laryngeal[a]	Esophageal[a]	Anogenital
Total with active disease	51/77 (66)	73/77 (95)	38/77 (49)	27/77 (35)	24/77 (31)	12/77 (16)	19/77 (25)
Non–high-risk active disease[b]	0	9/9 (100)	4/9 (44)	7/9 (78)	0	0	0
High-risk active disease[c,d]	51/68 (75)	64/68 (94)	34/68 (50)	20/68 (29)	24/68 (35)	12/68 (18)	19/68 (28)
Evidence of past disease[e]	4/77 (5)	1/77 (1)	1/77 (1)	2/77 (3)	0	1/77 (1)	1/77 (1)
Disease response to therapy[f]							
NR	2/51 (4)	0	0	1/27 (4)	1/24 (4)	0	0
PR	12/51 (24)	28/73 (38)	14/38 (37)	2/27 (7)	9/24 (38)	7/12 (58)	5/19 (26)
CR	37/51 (73)	45/73 (62)	24/38 (63)	24/27 (89)	14/24 (58)	5/12 (42)	14/19 (74)
Improvement (PR + CR)	49/51 (96)	73/73 (100)	38/38 (100)	26/27 (96)	23/24 (96)	12/12 (100)	19/19 (100)
Time to first CR, median (IQR), mo	19.3 (12.7-40.7)	17.0 (7.7-39.1)	12.9 (6.7-24.7)	8.0 (2.9-13.7)	19.7 (12.8-23.7)	24.3 (21.8-37.0)	13.9 (8.1-26.8)
Site-level relapse following CR at that site[g]							
≥1 Relapses	14/37 (38)	18/45 (40)	6/24 (25)	3/24 (13)	0	0	2/14 (14)
≥2 Relapses	2/37 (5)	5/45 (11)	1/24 (4)	0	0	0	0

Abbreviations: CR, complete remission; NR, no response; PR, partial response.

[a] Internal mucosal sites were monitored symptomatically.[25]

[b] Reclassifying anogenital disease as non–high-risk in sensitivity analysis did not meaningfully change remission outcomes.

[c] High-risk disease was defined as involvement of ocular, laryngeal, esophageal, or anogenital sites.[7]

[d] Evidence of past disease reflects sites with clinical or historical evidence of prior involvement that was no longer active at the time of initial evaluation; none of these patients experienced relapse.

[e] Disease response to therapy is reported among patients with active disease at each site. Initial site of presentation was not associated with multisite complete remission. Relapse risk differed according to initial site of disease presentation (global χ^2 test of independence: $P = .03$), with ocular-onset disease associated with greater odds of relapse at any site (odds ratio, 2.60; 95% CI, 1.05-8.12; χ^2 test $P = .02$).

[f] Relapses were seen in 28 patients. Some patients had relapses at multiple sites. Site-level relapse is reported as the number of patients experiencing disease recurrence among those who previously achieved CR at that site (No. with relapse/No. with CR).

cutaneous disease achieved CR faster than ocular (hazard ratio [HR], 3.08; 95% CI, 1.72-5.52; Holm-adjusted $P = .003$), oral (HR, 3.35; 95% CI, 1.97-5.71; Holm-adjusted $P < .001$), laryngeal (HR, 3.89; 95% CI, 1.90-7.95; Holm-adjusted $P = .004$), and esophageal disease (HR, 7.12; 95% CI, 2.50-20.30; Holm-adjusted $P = .004$), but not nasal or anogenital disease (eTable 2 in Supplement 1). Results were broadly similar in the shared-frailty sensitivity analysis. There was a statistically significant association between oral and nasal CR (odds ratio, 8.46; 95% CI, 2.25-31.83; Holm-adjusted $P < .001$). Oral CR (odds ratio, 8.60; 95% CI, 3.09-26.40; Holm-adjusted $P < .001$) was associated with achieving CR across all other involved sites (eTable 3 in Supplement 1). Demographic characteristics, disease severity, and immunopathologic findings were not associated with mCR.

Among 42 patients without mCR, 28 (67%) had persistent multisite activity. Oral and ocular were the most common final sites to remit, both among patients with 1 remaining active site (oral: 7 of 17 patients [41%]; ocular: 6 of 17 patients [35%]) and those who reached mCR (oral: 17 of 35 patients [49%]; ocular: 9 of 35 patients [26%]).

Site-level relapses occurred in 28 of the 64 patients (44%) who achieved CR at 1 or more sites, predominantly involving oral (18 of 28 patients [64%]) and ocular mucosa (14 of 28 patients [50%]), with some patients experiencing relapse at multiple sites (Table 2). Patients with relapses had longer follow-up (median [IQR], 88 [54-114] months vs 37 [16-60] months; $P < .001$). Among 35 patients achieving mCR, 18 (51%) experienced a relapse after a median (IQR) of 12 (11-26) months, similar to the time to first relapse among patients who never achieved mCR (median [IQR], 8 [6-22] months; $P = .52$). Relapses occurred equally during maintenance therapy and dose tapering. Of the 18 patients who experienced a relapse after achieving mCR, 12 (67%) subsequently regained mCR.

Rituximab-containing regimens were the most used systemic therapies (**Table 3**), with JAKi often used for rituximab-refractory disease. Serious adverse events occurred most frequently in patients receiving rituximab plus adjunctive conventional immunosuppressants (4 of 9 [44%]), dapsone monotherapy (4 of 12 [33%]), cyclophosphamide (2 of 6 [33%]), and JAKi (5 of 18 [28%]), including 1 death related to agranulocytosis-induced sepsis, and exceeded those observed with mycophenolate mofetil monotherapy (4 of 36 [11%]) (Table 3 and eTable 4 in Supplement 1).

Discussion

Achieving coordinated disease control across multiple mucosal surfaces remains a major therapeutic challenge in MMP. Although all patients in this study improved and 83% achieved CR at 1 or more involved sites, fewer than half achieved mCR, indicating that remission occurs asynchronously across involved sites. Faster mCR in non–high-risk disease may reflect its prevalence of cutaneous disease, which reached CR faster than several mucosal sites.

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Table 3. Treatment-Specific Clinical Responses, Adverse Events (AEs), and Serious AEs Among Patients With Multisite Mucous Membrane Pemphigoid[a]

Drug/combination therapy[b]	No./total No. (%)				
	mCR	PR	NR	Patients with AEs[c]	Patients with serious AEs[c]
Topical therapies only	4/6 (67)	2/6 (33)	0	0	0
Azathioprine monotherapy	1/7 (14)	3/7 (43)	3/7 (43)	1/7 (14)	1/7 (14)
Dapsone monotherapy	0	5/12 (42)	7/12 (58)	5/12 (42)	4/12 (33)
Methotrexate monotherapy	0	3/7 (43)	4/7 (57)	0	0
IVIG monotherapy	0	4/6 (67)	2/6 (33)	2/6 (33)	0
JAKi therapy[d]	5/18 (28)	13/18 (72)	0	10/18 (56)	5/18 (28)
Dupilimab monotherapy	0	2/2 (100)	0	0	0
MMF monotherapy	8/36 (22)	23/36 (64)	5/36 (14)	11/36 (31)	4/36 (11)
MMF + dapsone	0	1 (100)	0	0	0
Cyclophosphamide therapies					
Cyclophosphamide monotherapy	0	4/6 (67)	2/6 (33)	4/6 (67)	2/6 (33)
Cyclophosphamide + IVIG	0	1/1 (100)	0	0	0
RTX therapies					
RTX monotherapy	10/31 (32)	18/31 (58)	4/31 (13)	7/31 (23)	2/31 (6)
RTX + adjunctive conventional immunosuppressant[e]	2/7 (29)	5/7 (71)	0	3/7 (43)	3/7 (43)
RTX + IVIG therapies					
RTX + IVIG	4/24 (17)	18/24 (75)	2/24 (8)	8/24 (33)	5/24 (21)
RTX + IVIG + adjunctive conventional immunosuppressant[e]	1/2 (50)	1/2 (50)	0	2/2 (100)	1/2 (50)

Abbreviations: IVIG, intravenous immunoglobulin; JAKi, Janus kinase inhibitor; mCR, multisite complete remission; MMF, mycophenolate mofetil; NR, no response; PR, partial response; RTX, rituximab.

[a] Analyses were performed at the patient-drug level, with each patient counted once per therapy regardless of the number of therapies used or AEs experienced.

[b] Most patients with oral involvement received doxycycline and topical corticosteroids in addition to systemic therapies.

[c] AEs were defined as any untoward medical occurrence requiring clinical attention. Serious AEs were defined as events resulting in hospitalization, substantial disability, life-threatening consequences, or death, including severe cytopenias.

[d] Ten of 18 patients treated with JAKi were previously treated with a rituximab-based regimen with either PR or NR: 3 had received rituximab monotherapy, and 7 had received rituximab with IVIG.

[e] Seven of 9 patients receiving rituximab with a conventional immunosuppressant, with or without IVIG, had previously received a conventional immunosuppressant alone and received rituximab as escalation.

Previous cohorts have reported CR rates with rituximab ranging from 21% to 88%,[10,17,18,21] and favorable outcomes with other systemic agents,[8,9,12,13] but have not evaluated coordinated remission across all involved sites. Existing IBDCG remission definitions[7,25] appropriately quantify disease activity but do not distinguish localized from multisite disease, allowing patients with markedly different residual disease burdens to meet the same remission end points. Although mCR is not an IBDCG-defined outcome, the present findings suggest that it complements existing remission measures, as site-specific remission alone may overestimate coordinated disease control. Complementary reporting of multisite and site-specific remission may therefore provide a more complete assessment of treatment response while facilitating comparisons across studies enrolling patients with different patterns and extent of mucosal involvement. This distinction may be clinically important because persistent disease at a single site, particularly a high-risk site, may warrant treatment escalation despite remission elsewhere.

Although classified as low risk and often responsive to topical therapy alone,[7] oral disease was the most common barrier to mCR, accounted for the greatest relapse burden, and was the only site for which the association between site-level CR and mCR could be interpreted with sufficient precision. Persistent oral activity may reflect both active MMP and secondary periodontal inflammation resulting from gingival scarring, recession, and mucosal barrier disruption. Emerging evidence also implicates oral microbiome dysbiosis in perpetuating chronic mucosal inflammation,[26,27] while access to professional dental care varies[28] and may further influence disease control,[29] particularly in this predominantly Medicare-eligible cohort. Ocular disease likewise often remained active until late in the disease course despite high eventual remission rates, underscoring the importance of continued multidisciplinary surveillance. Clustering of oral and nasal CR may suggest shared regional disease behavior across contiguous mucosal surfaces.

Most patients required sequential escalation from conventional immunosuppressants to rituximab-based regimens and, for refractory disease, JAKi. Although rituximab-containing regimens produced high response rates, mCR remained limited, suggesting that B-cell-directed therapy alone may be insufficient to achieve global disease control. Combination regimens, particularly rituximab with intravenous immunoglobin, were therefore frequently used, underscoring the absence of standardized treatment algorithms and the need for individualized, site-directed management.

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Interpretation of rituximab-specific outcomes is complicated by heterogeneous induction and maintenance regimens reflecting differences in treatment protocols and payer authorization requirements. Increasingly restrictive rituximab policies[30-32] may further limit access to standardized therapy. These factors complicate comparisons with prior cohorts and may partially account for differences in reported remission rates.[10,18,33] Published rituximab regimens are also heterogeneous, although the highest reported remission rates have generally been observed with the regimen described by Bohelay et al[10]: 2 infusions of 1000 mg every 6 months until complete remission. Among patients with refractory disease, JAKi treatment was associated with clinical improvement despite multiple prior treatment failures, supporting a potential role as salvage therapy, although its preferential use in refractory disease limits conclusions regarding efficacy.

After site-level CR was achieved, relapses occurred in nearly half of patients, with oral and ocular diseases contributing the greatest overall relapse burden. Ocular-onset disease was associated with relapse at any site, whereas demographic characteristics, disease severity, and immunopathologic findings were not associated with achievement of mCR. Although previous studies have reported immunopathologic predictors of disease outcomes,[19] this study may have been underpowered to detect similar associations. Longer follow-up among patients who experienced a relapse may have increased the opportunity to detect recurrence.

Limitations

This study has several limitations. The racial composition of this cohort likely reflects referral and access bias rather than MMP epidemiology, as diagnosis often depends on access to ophthalmologic and dental care, both of which have well-documented disparities in the US.[34-36] Its retrospective single-center design introduces potential bias, including incomplete documentation, variable assessment across specialties, and overrepresentation of severe or refractory disease. Nonstandardized treatment selection, influenced in part by insurance authorization, limited treatment-specific analyses and may have contributed to differences in therapeutic exposure and remission patterns. Laryngeal and esophageal involvement were identified based on symptoms and specialty evaluation rather than routine endoscopic surveillance, underestimating subclinical disease, while the small number of patients with esophageal involvement limits interpretation of site-specific outcomes. Finally, defining relapse as recurrence after CR may underestimate clinically meaningful fluctuations in disease activity among patients who remained in partial remission, and the sample size and duration of follow-up may be insufficient to exclude slowly progressive cicatrization.

Conclusions

In this cohort study, fewer than half of patients with multisite MMP achieved simultaneous multisite remission despite high rates of site-specific response. Oral and ocular diseases were the primary drivers of persistent activity and relapse, supporting greater emphasis on site-directed assessment and management. Prospective studies incorporating standardized multisite outcome measures and stratified reporting by disease burden are needed to optimize treatment of multisite MMP.

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Author Contributions: Ms McAleer and Dr Dominguez had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: McAleer, Li, Dominguez.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical review of the manuscript for important intellectual content: All authors.
Statistical analysis: McAleer, Li, Dominguez.
Administrative, technical, or material support: La, Li, Cao, Dominguez.
Supervision: Li, Cao, Dominguez.

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REFERENCES

1. Rashid H, Meijer JM, Bolling MC, Diercks GFH, Pas HH, Horváth B. Insights into clinical and diagnostic findings as well as treatment responses in patients with mucous membrane pemphigoid: a retrospective cohort study. *J Am Acad Dermatol*. 2022;87(1):48-55. doi:10.1016/j.jaad.2021.11.061

2. Schmidt E, Zillikens D. Pemphigoid diseases. *Lancet*. 2013;381(9863):320-332. doi:10.1016/S0140-6736(12)61140-4

3. Zillikens D, Wever S, Roth A, Weidenthaler-Barth B, Hashimoto T, Bröcker EB. Incidence of autoimmune subepidermal blistering dermatoses in a region of central Germany. *Arch Dermatol*. 1995; 131(8):957-958. doi:10.1001/archderm.1995.01690200097021

4. Edalat C, Spangler M, Thorne J, Liberman P, Berkenstock M. Incidence and prevalence of mucous membrane pemphigoid with ocular involvement: a retrospective analysis using the TriNetX database. *Eye (Lond)*. 2025;39(18):3257-3261. doi:10.1038/s41433-025-04040-5

5. van Beek N, Kridin K, Bühler E, et al. Evaluation of site- and autoantigen-specific characteristics of mucous membrane pemphigoid. *JAMA Dermatol*. 2022;158(1):84-89. doi:10.1001/jamadermatol.2021.4773

6. Rashid H, Meijer JM, Diercks GFH, et al. Assessment of diagnostic strategy for mucous

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membrane pemphigoid. *JAMA Dermatol*. 2021;157(7):780-787. doi:10.1001/jamadermatol.2021.1036

7. Chan LS, Ahmed AR, Anhalt GJ, et al. The first international consensus on mucous membrane pemphigoid: definition, diagnostic criteria, pathogenic factors, medical treatment, and prognostic indicators. *Arch Dermatol*. 2002;138(3):370-379. doi:10.1001/archderm.138.3.370

8. Finn DJ, Graham C, Holt DJ, Kelly R, Rajlawat BP, Yesudian PD. Management of mucous membrane pemphigoid in a joint oral medicine-dermatology clinic. *Clin Exp Dermatol*. 2020;45(6):685-690. doi:10.1111/ced.14188

9. Johnson KB, Rosenbaum JT, Yarter JT, Broadbent T, Michels KSA. A 10-year review of the management of ocular mucous membrane pemphigoid: a private practice experience. *Cornea*. 2023;42(5):565-571. doi:10.1097/ICO.0000000000003071

10. Bohelay G, Alexandre M, Le Roux-Villet C, et al. Rituximab therapy for mucous membrane pemphigoid: a retrospective monocentric study with long-term follow-up in 109 patients. *Front Immunol*. 2022;13:915205. doi:10.3389/fimmu.2022.915205

11. Lytvyn Y, Rahat S, Mufti A, et al. Biologic treatment outcomes in mucous membrane pemphigoid: a systematic review. *J Am Acad Dermatol*. 2022;87(1):110-120. doi:10.1016/j.jaad.2020.12.056

12. Sami N, Bhol KC, Razzaque Ahmed A. Intravenous immunoglobulin therapy in patients with multiple mucosal involvement in mucous membrane pemphigoid. *Clin Immunol*. 2002;102(1):59-67. doi:10.1006/clim.2001.5150

13. Munyangango EM, Le Roux-Villet C, Doan S, et al. Oral cyclophosphamide without corticosteroids to treat mucous membrane pemphigoid. *Br J Dermatol*. 2013;168(2):381-390. doi:10.1111/bjd.12041

14. Nguyen C, Eziama E, Dominguez AR, Cao JH. Janus kinase inhibitors in the treatment of refractory cicatrizing conjunctivitis in pemphigoid. *Ocul Surf*. 2025;38:1-7. doi:10.1016/j.jtos.2025.05.002

15. Thorne JE, Woreta FA, Jabs DA, Anhalt GJ. Treatment of ocular mucous membrane pemphigoid with immunosuppressive drug therapy. *Ophthalmology*. 2008;115(12):2146-2152.e1. doi:10.1016/j.ophtha.2008.08.002

16. Saw VP, Dart JK, Rauz S, et al. Immunosuppressive therapy for ocular mucous membrane pemphigoid strategies and outcomes. *Ophthalmology*. 2008;115(2):253-261.e1. doi:10.1016/j.ophtha.2007.04.027

17. Maley A, Warren M, Haberman I, Swerlick R, Kharod-Dholakia B, Feldman R. Rituximab combined with conventional therapy versus conventional therapy alone for the treatment of mucous membrane pemphigoid (MMP). *J Am Acad Dermatol*. 2016;74(5):835-840. doi:10.1016/j.jaad.2016.01.020

18. Le Roux-Villet C, Prost-Squarcioni C, Alexandre M, et al. Rituximab for patients with refractory mucous membrane pemphigoid. *Arch Dermatol*. 2011;147(7):843-849. doi:10.1001/archdermatol.2011.54

19. Kridin K, van Beek N, Bühler E, et al. Characteristics associated with refractory course, blindness, and treatment strategy-related outcomes in patients with mucous membrane pemphigoid. *JAMA Dermatol*. 2023;159(2):198-203. doi:10.1001/jamadermatol.2022.5829

20. Shifera AS, Hong GH, Khan IR, Okeagu C, Thorne JE. Disease relapse after drug-free remission in ocular mucous membrane pemphigoid. *Am J Ophthalmol*. 2021;223:21-27. doi:10.1016/j.ajo.2020.09.029

21. Bamberger F, König IR, Gola D, Zillikens D, Sadik CD. Retrospective analysis of the long-term therapeutic effectiveness and safety profile of rituximab in the treatment of mucous membrane pemphigoid in a German university center between 2008 and 2019. *Front Immunol*. 2023;14:1180150. doi:10.3389/fimmu.2023.1180150

22. Eziama E, Nguyen C, Foster CS, Heydinger S, Cao JH. Novel grading scale for conjunctival inflammation in cicatrizing conjunctivitis associated with pemphigoid. *Ocul Immunol Inflamm*. 2025;33(4):649-653. doi:10.1080/09273948.2024.2434128

23. Thompson K, Johnny B, Eziama E, Dominguez AR, Cao JH. Mycophenolate mofetil for the treatment of cicatrizing conjunctivitis secondary to ocular pemphigoid. *AJO Int*. 2024;1(4):100078. doi:10.1016/j.ajoint.2024.100078

24. Johnny B, Thompson KN, Eziama E, Dominguez AR, Cao JH. Rituximab and intravenous immunoglobulin in the treatment of cicatrizing conjunctivitis associated with pemphigoid. *AJO Int*. 2025;2(1):100087. doi:10.1016/j.ajoint.2024.100087

25. Murrell DF, Marinovic B, Caux F, et al. Definitions and outcome measures for mucous membrane pemphigoid: recommendations of an international panel of experts. *J Am Acad Dermatol*. 2015;72(1):168-174. doi:10.1016/j.jaad.2014.08.024

26. Ye L, Ruan M, Xiao N, et al. Oral microbial dysbiosis and pathogenic functional shifts in mucosa-dominant pemphigus vulgaris and low-risk mucous membrane pemphigoid. *Oral Dis*. 2026;32(5):1347-1357. doi:10.1111/odi.70207

27. Huang X, Huang X, Huang Y, et al. The oral microbiome in autoimmune diseases: friend or foe? *J Transl Med*. 2023;21(1):211. doi:10.1186/s12967-023-03995-x

28. Allin S, Farmer J, Quiñonez C, et al. Do health systems cover the mouth? comparing dental care coverage for older adults in eight jurisdictions. *Health Policy*. 2020;124(9):998-1007. doi:10.1016/j.healthpol.2020.06.015

29. Garcia-Pola MJ, Rodriguez-López S, Fernánz-Vigil A, Bagán L, Garcia-Martín JM. Oral hygiene instructions and professional control as part of the treatment of desquamative gingivitis: systematic review. *Med Oral Patol Oral Cir Bucal*. 2019;24(2):e136-e144. doi:10.4317/medoral.22782

30. Rituxan-rituximab injection, solution. Prescribing information. Genentech; 1997. Updated January 6, 2025. Accessed May 26, 2026. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b172773b-3905-4a1c-ad95-bab4b6126563

31. Rituximab and biosimilars—non-oncologic indications. BlueCross BlueShield. Accessed September 25, 2026. https://secure.arkansasbluecross.com/members/report.aspx?policyNumber=2021034.

32. Rituximab. Micromedex. Accessed May 13, 2026. https://www.micromedexsolutions.com/home/dispatch/

33. Foster CS, Chang PY, Ahmed AR. Combination of rituximab and intravenous immunoglobulin for recalcitrant ocular cicatricial pemphigoid: a preliminary report. *Ophthalmology*. 2010;117(5):861-869. doi:10.1016/j.ophtha.2009.09.049

34. Rasendran C, Tye G, Knusel K, Singh RP. Demographic and socioeconomic differences in outpatient ophthalmology utilization in the United States. *Am J Ophthalmol*. 2020;218:156-163. doi:10.1016/j.ajo.2020.05.022

35. Hemmerich C, Jones G, Staggs J, Anderson RM, Bacani R, Vassar M. Inequities and research gaps in ophthalmology: a scoping review. *JAMA Ophthalmol*. 2023;141(1):63-70. doi:10.1001/jamaophthalmol.2022.5237

36. Testa A, Mijares L, Fu K, et al. Race disparities in dental care use from adolescence to middle adulthood in the USA. *J Epidemiol Community Health*. 2025;79(6):404-409. doi:10.1136/jech-2024-223202

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