pemphigoid (BP180, laminin 332), bullous pemphigoid (BP180, BP230), and epidermolysis bullosa acquisita (Col7). In line with our study, autoantibodies against these 4 antigens have previously been described in patients with anti-p200 pemphigoid in case reports and a case series.[3-5]

In 82 (33%) anti-p200 pemphigoid sera, reactivity against a single antigen in addition to p200/laminin γ1 was detected, and in 15 (6%) sera, reactivity against 2 additional antigens was detected (Fig 1). In some patients with dual autoantibody responses, the final diagnosis remained elusive because of no predominant autoantibody reactivity.

The study was limited by its retrospective, monocentric design and lack of clinical information that did not allow any correlation analyses between autoantibody specificities with a particular clinical phenotype, disease duration, or treatment responsiveness.

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REFERENCES

1. Zillikens D, Kawahara Y, Ishiko A, et al. A novel subepidermal blistering disease with autoantibodies to a 200-kDa antigen of the basement membrane zone. *J Invest Dermatol*. 1996;106:1333-1338.
2. Dainichi T, Kurono S, Ohyama B, et al. Anti-laminin gamma-1 pemphigoid. *Proc Natl Acad Sci U S A*. 2009;106:2800-2805.
3. Kikuchi K, Natsuga K, Shinkuma S, et al. Subepidermal blistering disease with 3 distinct autoantibodies: anti-BP230, anti-laminin gamma-1, and anti-laminin-332. *J Am Acad Dermatol*. 2011;65:878-880.
4. Kamata M, Fujita H, Hamanaka T, et al. Anti-laminin gamma1 pemphigoid accompanied by autoantibodies to laminin alpha3 and gamma2 subunits of laminin-332. *JAMA Dermatol*. 2013;149:1437-1439.
5. Lau I, Goletz S, Holtsche MM, Zillikens D, Fechner K, Schmidt E. Anti-p200 pemphigoid is the most common pemphigoid disease with serum antibodies against the dermal side by indirect immunofluorescence microscopy on human salt-split skin. *J Am Acad Dermatol*. 2019;81:1195-1197.

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Response of dermatomyositis to the antimalarial quinacrine: A retrospective cohort study

To the Editor: Quinacrine (QC) is an antimalarial taken with hydroxychloroquine or chloroquine to treat dermatomyositis (DM).[1,2] QC is prescribed at a constant dosage (100 mg/d), is well tolerated, and does not require blood or vision monitoring, but it may be associated with reversible skin yellowing.[2-4] In 2019, the US Food and Drug Administration placed the manufacturer of QC on import alert.[5] This is concerning because the lack of QC may increase reliance on steroids or immunosuppressants. To characterize the importance of the effects of QC on DM disease activity and quality of life, we present a retrospective study from a prospectively collected database of patients with DM.

Inclusion criteria included adult patients with an initial visit before starting QC, a follow-up visit at least 2 months after initiating QC, and no changes in immunosuppressive therapy between the 2 visits. Patients were followed up for up to 36 months. Data collected included Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity scores and the Skindex-29 parameters of symptoms, emotions, and photosensitivity. Patients were QC responders if the follow-up CDASI activity score decreased by at least 5 points or 20% from the initial visit. QC nonresponders did not meet either criteria. Wilcoxon signed rank tests and rank sum tests were performed to compare paired and unpaired variables, respectively, with a significance level of .05.

Of the 321 database patients, 20 started QC while in the database and had a follow-up visit

Table I. Paired comparison of CDASI activity scores and Skindex-29 scores

Category	QC responders (n = 10)	QC nonresponders (n = 10)
Age, y, median (IQR)	55.64 (48.33-62.71)	57.09 (52.38-61.09)
Weight, kg, median (IQR)	66.00 (65.77-77.57)	84.20 (75.41-98.00)
DM type, n (%)		
Classic	6 (60)	3 (30)
Amyopathic	4 (40)	7 (70)
Myositis autoantibodies (n)	Jo-1 (1)	Jo-1 (1)
	SSA (1)	Negative (1)
	TIF1-γ (1)	
	RNP (1)	
	Negative (1)	
Other antimalarial use (n)	Hydroxychloroquine (8)	Hydroxychloroquine (9)
	Chloroquine (1)	Chloroquine (1)
	None (1)	None (0)
Other systemic medications at QC initiation (n)	Any systemic drug (9)	Any systemic drug (7)
	Prednisone (1)	Prednisone (3)
	Methotrexate (3)	Methotrexate (4)
	Azathioprine (0)	Azathioprine (1)
	Mycophenolate mofetil (3)	Mycophenolate mofetil (1)
	IVIG (1)	IVIG (0)
	None (3)	None (4)
Adverse effects from quinacrine (n)	Yellowing of skin (1)	Rash (1)
	None (9)	Yellowing of skin (1)
		None (8)
Time between initial and follow-up visit, mo, median (IQR)	5.88 (2.91-12.81)	5.18 (2.47-13.38)
Median time from disease onset to start of QC, mo, median (IQR)	87.82 (18.76-141.53)	46.48 (20.00-61.52)
CDASI activity, median (IQR)		
Initial visit	23 (12-28)	17 (11-20)
Follow-up	10 (4-16)	20 (15-23)
P value	.006*	.052
Skindex-29 symptoms, median (IQR)		
Initial visit	53.57 (45.54-68.75)	39.29 (25-57)
Follow-up	41.07 (23.21-49.11)	42.86 (25-68)
P value	.058	>.999
Skindex-29 emotions, median (IQR)		
Initial visit	62.50 (56.87-82.50)	37.50 (30-53)
Follow-up	38.75 (30.00-50.63)	37.50 (20-53)
P value	.023*	.767
Skindex-29 photosensitivity, median (IQR)		
Initial visit	50.00 (28.13-84.38)	31.25 (25-84)
Follow-up	50.00 (15.63-71.88)	56.25 (28-94)
P value	.722	.507
Change in immunosuppressive dosing after follow-up visit, n		
Started or dosage increased	2	3
Dosage decreased	5	3
Dosage unchanged	2	1
No immunosuppressives started	1	3

CDASI, Cutaneous Dermatomyositis Disease Area and Severity Index; *DM*, dermatomyositis; *IQR*, interquartile range; *IVIG*, intravenous immunoglobulin; *QC*, quinacrine.
*Statistical significance, where $P < .05$.

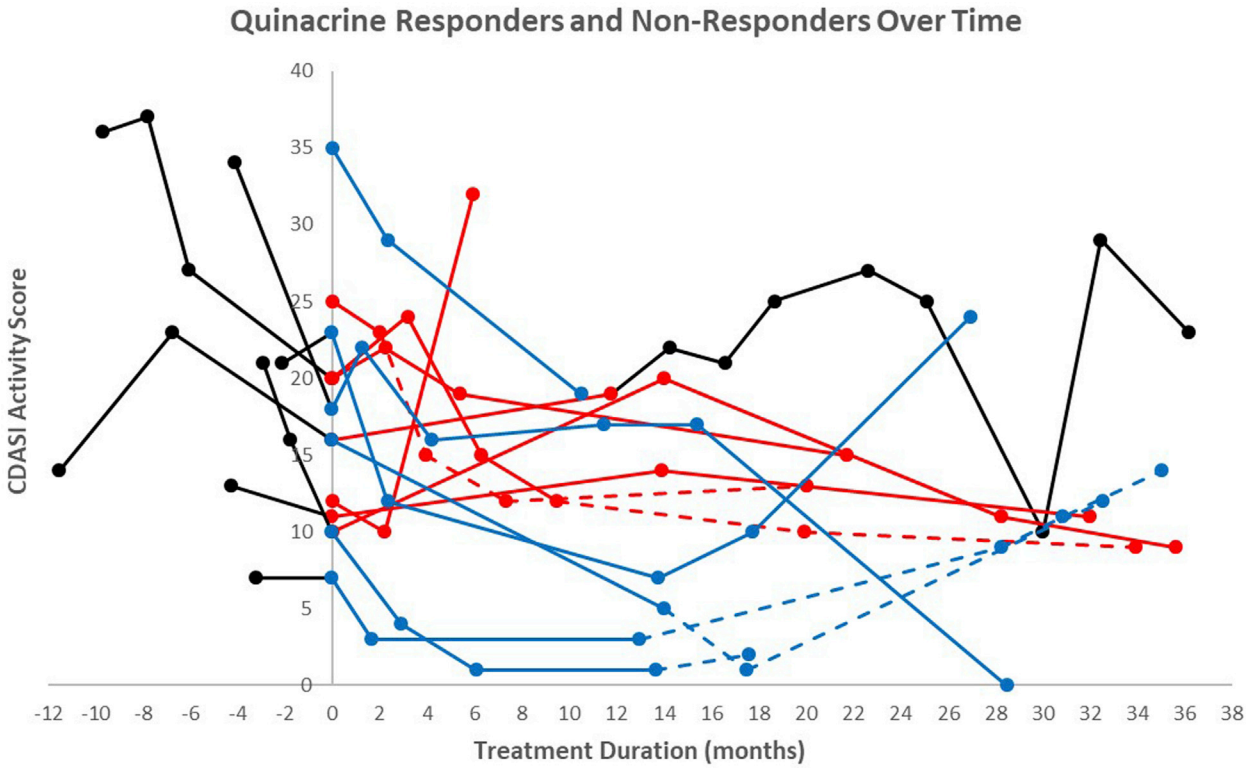

Fig 1. CDASI activity relative to starting QC (at 0 months) among QC responders (blue) and QC nonresponders (red). Black lines indicate when QC was discontinued. Dashed lines indicate when immunosuppressive dosage was decreased. *CDASI*, Cutaneous Dermatomyositis Disease Area and Severity Index; *QC*, quinacrine.

after at least 2 months (10 QC responders, 10 QC nonresponders). Twelve patients (6 QC responders, 6 QC nonresponders) had more than 2 visits within 36 months of initiating QC. Antimalarial use was similar for both treatment groups (Table I). There was no significant difference in age ($P = .739$), time between visits ($P = .821$), and time from disease onset to treatment initiation ($P = .436$) for QC responders and nonresponders. There was a nonsignificant but notable difference in the weights of QC responders and nonresponders (66.00 vs 84.20 kg; $P = .1564$). Four of 5 QC responders with myositis panel results were autoantibody positive, compared to 1 of 2 nonresponders. Adverse effects were infrequent, with 1 QC responder experiencing skin yellowing and 2 QC nonresponders experiencing skin yellowing and rash development.

QC responders experienced a decrease in the CDASI activity score (23 to 10; $P = .006$) and the Skindex-29 factors of symptoms ($P = .058$) and emotions ($P = .023$) but not photosensitivity ($P = .722$) (Table I). Such changes were not observed for QC nonresponders. Among QC responders (Fig 1), the CDASI activity score decreased for approximately 14 months, after which activity appeared to increase. This may coincide with immunosuppressant dosage reduction for some patients. Immunosuppressant dosage reduction was more frequent among QC responders (Table I).

Despite the sample size, our study shows that quinacrine is beneficial for 50% of patients with DM not responding to or tolerating hydroxychloroquine. QC response may depend on baseline disease activity, weight, and autoantibody status. The loss of quinacrine highlights the paucity of nonimmunosuppressive treatments for DM and the need for new drugs to improve the quality of life of patients with this condition.

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REFERENCES

1. Anyanwu C, Chansky PB, Fent R, Carr K, Okawa J, Werth VP. The systemic management of cutaneous dermatomyositis: results of a stepwise strategy. *Int J Womens Dermatol*. 2017;3(4):189-194.
2. Mittal L, Werth VP. The quinacrine experience in a population of patients with cutaneous lupus erythematosus and dermatomyositis. *J Am Acad Dermatol*. 2017;77(2):374-377.
3. Lam C, Vleugels RA. Management of cutaneous dermatomyositis. *Dermatol Ther*. 2012;25(2):112-134.
4. Mittal L, Zhang L, Feng R, Werth VP. Antimalarial drug toxicities in patients with cutaneous lupus and dermatomyositis: a retrospective cohort study. *J Am Acad Dermatol*. 2018;78(1):100-106.e1.
5. American College of Rheumatology. Quinacrine shortage & what the ACR is doing about it. 2019. Available at: https://www.the-rheumatologist.org/article/quinacrine-shortage-what-the-acr-is-doing-about-it/. Accessed February 25, 2020.

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A phase 2, double-blinded, placebo-controlled trial of toll-like receptor 7/8/9 antagonist, IMO-8400, in dermatomyositis

To the Editor: Dermatomyositis (DM) is a rare inflammatory disease of muscle and skin. DM severity is thought to be driven, in part, by type I interferon signaling.[1] Because interferon is primarily induced by toll-like receptors (TLRs) 7/9, we hypothesized that antagonizing TLR7/9 could improve DM disease activity.[2,3]

Table I. Baseline characteristics of the intent-to-treat population

Characteristics	Placebo	IMO-8400 0.60 mg/kg	IMO-8400 1.8 mg/kg
n	11	9	10
Age, y, mean (SD)	51.3 (10.6)	48.3 (14.2)	54.6 (14.1)
Sex, n (%)			
Female	7 (63.6)	7 (77.8)	9 (90.0)
Male	4	2	1
Race, n (%)			
White	11 (100)	8 (88.9)	9 (90.0)
Black or African American	0	1 (11.1)	1 (10.0)
CDASI, n (%)			
15-20	1 (9.1)	0	2 (20.0)
≥21	10 (90.9)	9 (100)	8 (80.0)
CDASI activity score, mean (SD)	30.2 (9.8)	33.0 (8.4)	33.5 (14.7)
Treatment-concomitant drugs, n (%)			
Systemic corticosteroids* (%)	8 (72.7)	5 (55.6)	5 (50.0)
DMARDs† (%)	5 (45.5)	6 (66.7)	6 (60.0)
Immunoglobulins (%)	1 (9.1)	0	1 (10.0)

CDASI, Cutaneous Dermatomyositis Disease Area and Severity Index; *DMARD*, disease-modifying antirheumatic drugs; *SD*, standard deviation.
*Methylprednisolone, prednisolone, and prednisone.
†Azathioprine, leflunomide, methotrexate, mycophenolate mofetil, and mycophenolic acid.

We conducted a phase 2, multicenter, double-blind, randomized, placebo-controlled trial of IMO-8400, an oligonucleotide antagonist of TLR7/8/9, in DM.[4,5] Thirty patients with Cutaneous Dermatomyositis Disease Area and Severity Index version 2 (CDASIv2) scores of 15 or greater were enrolled between November 2015 and June 2018. Patients were allowed to remain on stable prednisone (≤20 mg/d) and up to 1 immunomodulatory therapy from a prespecified list (Table I and Supplemental Table 1, *A* and *B*; available via Mendeley at https://doi.org/10.17632/f9vx46p3fc.1).

Participants were stratified into 2 groups by CDASIv2 activity score (15-20 vs ≥21) and randomized 1:1:1 to receive weekly subcutaneous injections of IMO-8400 0.6 mg/kg, IMO-8400 1.8 mg/kg, or placebo for 24 weeks. Because IMO-8400 is associated with injection site reactions, the primary outcome used a modified CDASIv2 activity score (CDASI-a) excluding the injection site.

Secondary assessments included the Manual Muscle Test 8 (MMT8).