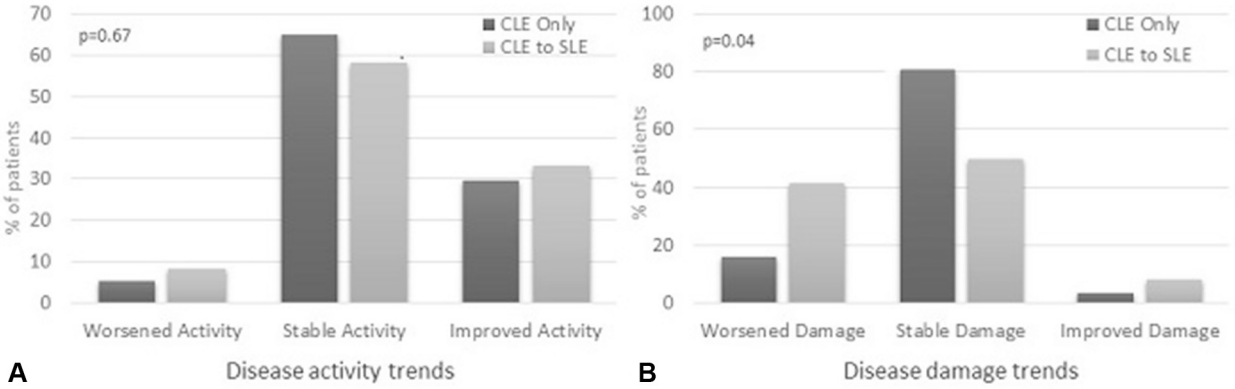

Fig 1. Frequencies of the CLE-only and CLE-to-SLE patients with worsened, stable, or improved disease activity or damage over time. Percentages of those with (**A**) worsened, stable, or improved disease activity or (**B**) damage trends were calculated for patients with CLE only and those with CLE that progressed to SLE. To assess disease activity or damage trends over time, average change scores for CLASI activity and damage were calculated as the mean difference between each patient's follow-up visit scores and baseline visit scores. An average change score of -3 or less indicates improvement, a score of -3 to 3 indicates stability, and a score of 3 or greater indicates worsening of disease activity or damage. *P* values were calculated by Fisher's exact test. *CLE*, Cutaneous lupus erythematosus; *CLASI*, Cutaneous Lupus Erythematosus Disease Area and Severity Index; *SLE*, systemic lupus erythematosus.

from Viela Bio and Beacon Bioscience as a consultant. Dr Walocko, Ms Black, Mr Anderson, Dr Li, and Ms Adams-Huet have no conflicts of interest to declare.

IRB approval status: Reviewed and approved by University of Texas Southwestern Medical Center IRB.

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Management of immune checkpoint inhibitor–induced bullous pemphigoid

To the Editor: Management of immune checkpoint inhibitor (ICI)–mediated bullous pemphigoid (BP) is challenging because high doses of systemic corticosteroids, a first-line therapy for classic BP, may jeopardize immunotherapy.[1-3]

We reviewed the records of patients who received ICI and developed BP from January 1, 2017, through October 30, 2019. BP diagnosis was based on clinical, histologic, and immunologic criteria. At baseline, 88.2% (median, 56 UA/mL) and 67.4% (median, 38 UA/mL) of patients had positive results on BP180 and BP230 enzyme-linked immunosorbent assays, respectively. We recorded clinical data, therapeutic intervention, and outcome. BP and pruritus severities were classified using the Common Terminology Criteria for Adverse Events (Fig 1). Thirteen individuals were identified (Table I). The average time from BP onset to diagnosis was 20.6 days. One patient was treated with potent topical steroids, and 12 of 13 individuals were treated with low-dose (0.3-0.5 mg/kg/d; range, 15-40 mg/d) prednisolone. In 11 of 12 treated with systemic steroids, BP was adequately controlled, whereas in 1 of 12 a dose increase to 0.7 mg/kg/d was required (patient 12). The average cumulative prednisone dose and mean time to control of BP were 419.2 mg and 15.8 days,

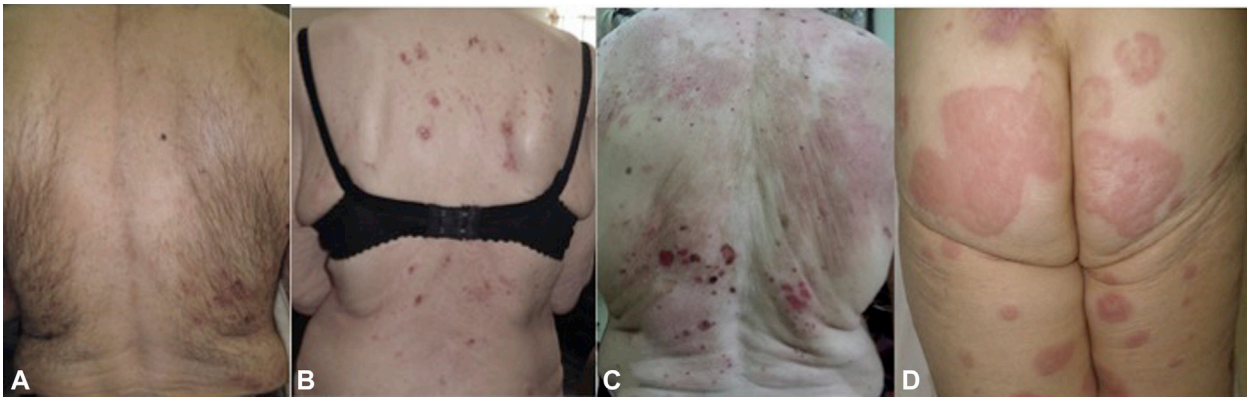

Fig 1. Typical examples of (**A**) grade 1, (**B**) grade 2, and (**C**) grade 3 toxicity based on the Common Terminology Criteria for Adverse Events. (**D**) A patient with pre-bullous BP, characterized by the presence of urticarial plaques and pruritus, without clinically evident vesicles and bullae.

respectively. ICI was unaltered in 7 (patients 2-5, 8, 10, and 13), temporarily interrupted in 2 (patients 1 and 6), and permanently discontinued in 4 (patients 7, 9, 11, and 12). Seven patients who continued ICI remained free of BP with an average prednisolone dose of 2.5 to 5 mg/d. Two of them stopped ICI because of cancer progression. The 2 patients who temporarily discontinued ICI because of BP missed 2 doses but reinitiated immunotherapy afterward. Four months later, while receiving prednisolone 20 mg/d, 1 of them experienced BP recurrence, and nivolumab was permanently terminated (patient 1). The second individual stopped pembrolizumab after 1 year because of progressive disease. Oncologists discontinued ICI in 4 patients, and despite adequate control with low prednisolone doses in 3 of them, they did not reinitiate it because of risk of recurrence. The latter fact highlights the need for better collaboration between the involved specialists.

Nelson et al[4] showed that development of BP might indicate a favorable response to ICI. On the other hand, Faje et al[1] concluded that prednisolone doses above 7.5 mg/d might pertain to worse survival. In this scenario, interventions that secure BP control without interfering with ICI are desirable. In our series, the 7 individuals who continued ICI received more than 7.5 mg/d for only a short period of time (mean, 20.6 d), and the mean average dose for the total treatment time was 4.1 mg/d.

In a review, Lopez et al[5] reported 21 cases of ICI-induced BP managed with systemic steroids with higher doses compared to ours (range, 0.5-2.0 mg/kg) or in combination with other agents.[5]

Our results indicate that early intervention in ICI-induced BP may allow adequate management with comparatively low doses of steroids. Grade 1/2 eruptions can be managed with low doses of prednisolone and potent topical steroids, without impeding ICI. In more severe cases, we recommend starting with a low dose of systemic prednisolone, without altering ICI. If there is no response, the results of our small cohort indicate that BP can be controlled by increasing prednisolone to 0.7 mg/kg while withholding 1 to 2 ICI doses. After achieving control of BP, ICI can be reinitiated.

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Table I. Patient and disease characteristics at baseline, management, and impact of toxicity on the oncologic treatment

Patient	Age, y	Sex	Diagnosis	ICI, type/ frequency, wk	Time receiving treatment, mo	Time to diagnosis, d*	Time to control of BP, d†	Cumulative prednisone dose until control of BP, mg	Other toxicity	Pre-bullous rash	Mucosae	Pruritus grade	BP grade	Hospitalization	BP treatment	Outcome on ICI
1	60	M	NSCLC	N/2	1	37	16	420	No	Yes	Yes	2	3	Yes	LD (40 mg max)	Withholding of 2 doses and reinitiation for 4 months, recurrence of BP Discontinued ICI
2	77	M	NSCLC	N/2	3	27	21	420	No	Yes	No	3	3	No	LD (20 mg max)	Continued ICI
3	67	M	NSCLC	N/2	3	12	7	—	No	No	No	2	1	No	Topical steroids	Continued ICI for 3 months Stopped because of PD
4	65	F	Thymoma	N/2	5	16	9	180	No	No	No	1	1	No	LD (20 mg max)	Continued ICI
5	73	M	Urothelial Ca	N/2	3	23	20	400	No	Yes	No	3	3	No	LD (20 mg max)	Continued ICI
6	69	F	Renal	N/2	4	14	14	210	No	No	No	2	2	No	LD (20 mg max)	Withholding of 2 doses and reinitiation for 1 year Stopped because of PD
7	71	F	Melanoma	N/2	2	28	18	580	No	No	No	2	3	Yes	LD (40 mg max)	Discontinued ICI
8	70	M	NSCLC	P/3	4	9	12	240	No	Yes	No	2	1	No	LD (20 mg max)	Continued ICI
9	58	M	Merkel	P/3	3	20	20	600	No	Yes	No	2	2	Yes	LD (40 mg max)	Discontinued ICI
10	64	M	NSCLC	N/2	3	15	9	180	No	Yes	No	3	1	No	LD (20 mg max)	Continued ICI
11	61	M	Melanoma	P/3	4	25	14	380	Vitiligo	Yes	No	2	2	Yes	LD (40 mg max)	Discontinued ICI
12	75	F	Melanoma	N/2	5	25	30	1200	Vitiligo	No	No	3	1	Yes	HD (70 mg max)	Discontinued ICI

13	72	M	NSCLC	P/4	4	17	16	640	No	Yes	3	3	Yes	LD (40 mg max)	Continued ICI for 1y Stopped due to PD

BP, Bullous pemphigoid; *F*, female; *HD*, high dose (0.6-0.8 mg/kg); *ICI*, immune checkpoint inhibitor; *LD*, low dose (0.3-0.5 mg/kg); *M*, male; *max*, maximum; *N*, nivolumab; *NSCLC*, non–small cell lung cancer; *P*, pembrolizumab; *PD*, progressive disease.
*Time from the clinical appearance of BP signs and symptoms to BP diagnosis and treatment initiation.
†Time from treatment initiation to control of BP activity.

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Efficacy and safety of hydroxychloroquine for treatment of patients with rosacea: A multicenter, randomized, double-blind, double-dummy, pilot study

To the Editor: Rosacea is a chronic inflammatory skin disease characterized by facial erythema, papules, pustules, telangiectasia, and flushing.[1] Oral doxycycline has been approved as a first-line systemic treatment for papulopustular rosacea,[2] but it is not consistently effective and is occasionally associated with gastrointestinal, neurologic, and infection-related adverse effects.[3] Hydroxychloroquine (HCQ) is currently used to treat patients with systemic autoimmune diseases[4] and is considered safe for use during pregnancy.[5] In this pilot study, we investigated the efficacy and safety of HCQ for treating rosacea.

Overall, 66 patients with rosacea enrolled, and 58 (87.8%) completed the multicenter, randomized, double-blind, double-dummy, pilot study. They were randomized to receive oral HCQ (200 mg twice daily) or doxycycline (100 mg once daily) and their respective placebos for 8 weeks, without any topical therapies, and were assessed at 4 visits (baseline and weeks 4, 8, and 20). A per-protocol analysis was undertaken. The study was approved by the Xiangya Hospital Institutional Review Board, Central South University (Clinical Trial Registration: ChiCTR-IPR-17012224).

Baseline characteristics were similar between the 2 groups (Table I). At week 4, the 2 groups had achieved similar improvement in erythema and papules, but the noninferiority was inconclusive ($P > .05$) (Table II). At the end of week 8, the