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.

REFERENCES

1. Faje AT, Lawrence D, Flaherty K, et al. High-dose glucocorticoids for the treatment of ipilimumab-induced hypophysitis is associated with reduced survival in patients with melanoma. *Cancer*. 2018;124:3706-3714.
2. Siegel J, Totonchy M, Damsky W, et al. Bullous disorders associated with anti-PD-1 and anti-PD-L1 therapy: a retrospective analysis evaluating the clinical and histopathologic features, frequency, and impact on cancer therapy. *J Am Acad Dermatol*. 2018;79:1081-1088.
3. Ujiie H, Iwata H, Yamagami J, et al. Japanese Guidelines for the management of pemphigoid (including epidermolysis bullosa acquisita). *J Dermatol*. 2019;46:1102-1135.
4. Nelson CA, Singer S, Chen T, et al. Bullous pemphigoid after anti-PD-1 therapy: a retrospective case-control study evaluating impact on tumor response and survival outcomes [e-pub ahead of print]. *J Am Acad Dermatol*. https://doi.org/10.1016/j.jaad.2019.12.068. Accessed December 17, 2020.
5. Lopez AT, Khanna T, Antonov N, Audrey-Bayan C, Geskin L. A review of bullous pemphigoid associated with PD-1 and PD-L1 inhibitors. *Int J Dermatol*. 2018;57:664-669.

https://doi.org/10.1016/j.jaad.2020.05.045

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

Table I. Demographic and baseline clinical characteristics of patients with rosacea*

Characteristics	HCQ (n = 28)	Doxycycline (n = 30)	*P*
Sex, No. (%)			.386
Men	5 (17.9)	3 (10)	
Women	23 (82.1)	27 (90)	
Age, mean (SD), y	32.7 (10.0)	34.8 (11.2)	.462
Height, median (IQR), cm	162.25 (158, 167.5)	160 (158, 165)	.503
Weight, median (IQR), kg	58 (50, 62.75)	52.5 (47, 60)	.379
SBP, median (IQR), mm Hg	120 (110, 121)	117.5 (105, 121.75)	.728
DBP, median (IQR), mm Hg	75 (70, 90)	70 (60, 76.75)	.641
Baseline RosQol, median (IQR), score	52 (43, 60.75)	45.5 (34.5, 59.75)	.864
CEA, No. (%)			
Mild	3 (10.71)	4 (13.33)	
Moderate	15 (53.57)	19 (63.33)	
Severe	10 (35.71)	7 (23.33)	
IGA, No. (%)			
Mild	9 (32.14)	7 (23.33)	
Moderate	13 (46.43)	17 (56.67)	
Severe	6 (21.43)	6 (20.00)	

CEA, Clinician's Erythema Assessment; *DBP*, diastolic blood pressure; *HCQ*, hydroxychloroquine; *IGA*, Investigator's Global Assessment; *IQR*, interquartile range; *RosQol*, Rosacea-specific Quality-of-Life instrument; *SBP*, systolic blood pressure.
*The enrolled patients with rosacea had fixed erythema and papules, with or without pustules. Patients with phymatous change and ocular symptoms were excluded.

Table II. Primary and secondary outcomes at week 4 and week 8

Clinical outcomes	HCQ (n = 28)	Doxycycline (n = 30)	Difference, % (90% CI)	*P* value
4 weeks				
Primary outcomes				
CEA success, No. (%)*†	19 (67.86)	21 (70.00)	−2.1 (−22.2 to 17.9)	.259
Change in RosQoL, median (IQR)‡	8.00 (−1.75, 13.50)	9.00 (0.75, 16.00)	−1.5 (−6.0 to 3.0)	.252
Secondary outcomes				
IGA success, No. (%)*§	22 (78.57)	24 (80.00)	−1.4 (−18.9 to 16.1)	.211
Excellent improvement, No. (%)*‖	13 (46.42)	19 (63.33)	−16.9 (−38.1 to 43.0)	.704
8 weeks				
Primary outcomes				
CEA success, No. (%)*†	25 (89.28)	26 (86.67)	2.6 (−11.4% to 16.6%)	.193
Change in RosQoL, median (IQR)‡	13.00 (4.25, 18.75)	10.50 (1.75, 19.00)	2.00 (−3.00 to 7.00)	.042
Secondary outcomes				
IGA success, No. (%)*§	23 (82.14)	28 (93.33)	−11.2 (−25.3 to 2.9)	.555
Excellent improvement, No. (%)*‖	22 (78.57)	21 (70.00)	8.5 (−10.2 to 27.3)	.052

CEA, Clinician's Erythema Assessment; *CI*, confidence interval; *HCQ*, hydroxychloroquine; *IGA*, Investigator's Global Assessment; *IQR*, interquartile range values; *RosQol*, Rosacea-specific Quality-of-Life instrument.
*Noninferiority test using *Z* test, margin = 10%.
†CEA success: defined as a decrease of at least 1 point.
‡Noninferiority test using Mann-Whitney *U* test, margin = 3.2.
§IGA success: defined as an IGA score of "clear" or "almost clear" (IGA: 0 or 1).
‖Excellent improvement: defined as a CEA score of "clear" or "almost clear" (CEA: 0 or 1).

difference in changes in total scores on the Rosacea-Specific Quality-of-Life instrument in the HCQ group was noninferior to that in the doxycycline group, with a difference between the 2 groups of 2.0 (90% confidence interval, −3.0 to 7.0; $P = .042$). However, owing to the small sample size, no noninferior results were seen in the Clinician's Erythema Assessment success (at least 1-point decrease) rate in the HCQ and doxycycline groups (89.28% vs 86.67%, $P = .193$). Similar inconclusive noninferior results were seen in the Investigator's Global Assessment success of "clear" or "almost clear" rates for HCQ (82.14%) vs doxycycline (93.33%; $P = .555$). Another important outcome, excellent improvement rate (a Clinician's Erythema Assessment score of "clear" or "almost clear") in the

HCQ group was borderline noninferior to that in the doxycycline group (78.57% vs 70.00%, $P = .052$).

During the study, 18 patients reported 31 adverse events, and the proportion of patients with adverse events was low and similar between the HCQ (28.5%) and doxycycline (33.3%) groups. The most common adverse events were dry skin (14.3%), dry eye (7.1%), and dizziness (7.1%) in HCQ group and dry skin (16.7%) and flatulence (10.0%) in doxycycline group. Only 1 patient in the doxycycline group discontinued treatment owing to a severe adverse event (thrombocytopenia). During the follow-up of 12 weeks, there were 4 cases of recurrence in the HCQ group and 3 in the doxycycline group.

This study had some limitations, including the small sample size and the fact that some outcomes could not reach conclusive noninferior inference.

To conclude, this preliminary study suggested that HCQ can produce improvement of rosacea. Considering the general safety of HCQ during pregnancy, it can be better promoted in female patients with rosacea. Our findings should be replicated in studies with larger populations.

We thank the following dermatology centers in China—Xiangya Hospital of Central South University, Guangdong Provincial Dermatology Hospital, Shandong Provincial Hospital of Dermatology, Shanghai Dermatology Hospital, and The Third Affiliated Hospital of Sun Yat-Sen University—for their work on this project and, in particular, the patients who participated in this trial.

Ben Wang, MD,[a,b] Xin Yuan, MD,[a] Xin Huang, MD,[c] Yan Tang, MD,[a,b] Zhixiang Zhao, MD,[a,b] Bin Yang, MD,[d] Baoqi Yang, MD,[e] Yue Zheng, MD,[f] Chao Yuan, MD,[g] Hongfu Xie, MD, PhD,[a,b,b] and Ji Li, MD, PhD[a,b,b,i]

From the Department of Dermatology[a] and the National Clinical Research Center for Geriatric Disorders,[b] Xiangya Hospital, Central South University, Changsha, Hunan; the Department of Preventive Medicine, the Medicine School of Hunan Normal University, Changsha, Hunan[c]; Guangdong Provincial Dermatology Hospital, Guangzhou, Guangdong[d]; Shandong Provincial Hospital of Dermatology, Jinan, Shandong[e]; Department of Dermatology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, Guangdong[f]; Shanghai Dermatology Hospital, Shanghai[g]; the Key Laboratory of Organ Injury, Aging and Regenerative Medicine of Hunan Province, Central South University, Changsha, Hunan[b]; and the Center for Molecular Medicine, Xiangya Hospital, Central South University, Changsha, Hunan, China.[i]

Funding sources: This work was supported by grants from the National Natural Science Foundation of China (81703149, 81602784, and 81502709) and the Science and Technology Aid Program of Xinjiang Uygur Autonomous Region (2019E0289).

Conflicts of interest: None disclosed.

IRB approval status: Reviewed and approved by the Xiangya Hospital Institutional Review Board (approval #201701001).

Reprints not available from the authors.

Correspondence to: Ji Li, MD, PhD, Department of Dermatology, Xiangya Hospital, Central South University, Xiangya Rd, Kaifu District, Changsha 410008, China

E-mail: liji_xy@csu.edu.cn

Correspondence to: Hongfu Xie, MD, PhD, Department of Dermatology, Xiangya Hospital, Central South University, Xiangya Rd, Kaifu District, Changsha 410008, China

E-mail: xiehongfu1964@aliyun.com

REFERENCES

1. Gallo RL, Granstein RD, Kang S, et al. Standard classification and pathophysiology of rosacea: the 2017 update by the National Rosacea Society Expert Committee. *J Am Acad Dermatol*. 2018;78(1):148-155.
2. van Zuuren EJ, Fedorowicz Z, Tan J, et al. Interventions for rosacea based on the phenotype approach: an updated systematic review including GRADE assessments. *Br J Dermatol*. 2019;181(1):65-79.
3. van der Linden MMD, van Ratingen AR, van Rappard DC, Nieuwenburg SA, Spuls PI. DOMINO, doxycycline 40 mg vs. minocycline 100 mg in the treatment of rosacea: a randomized, single-blinded, noninferiority trial, comparing efficacy and safety. *Br J Dermatol*. 2017;176:1465-1474.
4. Frances C, Cosnes A, Duhaut P, et al. Low blood concentration of hydroxychloroquine in patients with refractory cutaneous lupus erythematosus: a French multicenter prospective study. *Arch Dermatol*. 2012;148:479-484.
5. Costedoat-Chalumeau N, Amoura Z, Huong DL, Lechat P, Piette JC. Safety of hydroxychloroquine in pregnant patients with connective tissue diseases. Review of the literature. *Autoimmun Rev*. 2005;4:111-115.

https://doi.org/10.1016/j.jaad.2020.05.050

The role of thymus and activation-regulated chemokine as a marker of severity of atopic dermatitis

To the Editor: Serum thymus and activation-regulated chemokine (TARC) is reported to be an objective biomarker of the severity of atopic dermatitis (AD), with a high sensitivity and specificity.[1-3] To study these aspects, 103 case