Table II. Factors influencing achieving high rating*

Predictor	Higher rating (> 4.15 average score) Odds ratios	95% CI	*P* value
Intercept	0.87	0.29-2.63	.8
Sex: male	1.56	0.76-3.20	.226
Density: most dense	2.61	1.01-6.79	.048
Years of experience	0.96	0.94-0.99	.006
Observations	163		
Cox & Snell R^2/ Nagelkerke R^2	0.070/0.094		

CI, Confidence interval.
*The effect of sex, location, and years of experience on the odds ratio of achieving a rating above the 50th percentile.

Most patients gave high ratings and expressed satisfaction in their reviews. Although our study found no bias in ratings toward a particular sex, patient reported greater satisfaction with younger dermatologists and those in more dense areas. Younger physicians in urban areas may use newer technologies, have more resources available, and spend more time with patients as they build their practices.

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Bullous disorders associated with PD-1 and PD-L1 inhibitors: Pharmacovigilance analysis of the United States Food and Drug Administration Adverse Event Reporting System from the Research on Adverse Drug Events And Reports Program

To the Editor: Although bullous disorders (BDs) are increasingly recognized as associated with programmed cell death 1 (PD-1) inhibitors (nivolumab, pembrolizumab) and PD ligand 1 (PD-L1) inhibitors (atezolizumab, avelumab, durvalumab), the characterization of BD events in the full prescribing information for these agents is not well delineated as represented by the full prescribing information for nivolumab (PD-1)[1] and avelumab (PD-L1).[2]

When used as monotherapy, the most recent full prescribing information for these agents, collectively through 2018, simply reports dermatologic events as "rash, all grades" (up to 40% of patients) and "rash, grades 3-4" (up to 1.6% of patients). Moreover, although "rash, grades 3-4" is variously described, it is not specific to BDs. Yet, a retrospective analysis of data from 853 oncodermatology patients, each of whom were treated with 1 of the 5 PD-1 or PD-L1 inhibitors, found nearly 1% of patients experienced a BD.[3]

We therefore aimed to determine whether an association exists between PD-1/PD-L1 agents and BDs in the United States Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS). We used Research on Adverse Drug Events And Reports Program (RADAR) methodology[4] to search FAERS from the first FDA approval date (Table I)[5] to the last quarter for which data were available (first quarter of 2018).

The FAERS database was searched using Medical Dictionary for Regulatory Activities (MedDRA MSSO, McLean, VA) BD terms (pemphigoid, pemphigus, and bullous dermatitis) for patients receiving PD-1 (nivolumab, pembrolizumab) and PD-L1 inhibitors (atezolizumab, avelumab, durvalumab) and linked to a serious outcome (death, disability, hospitalization, life-threatening, required intervention to prevent permanent impairment/damage, or other serious). The proportional reporting ratio (PRR) was

Table I. The United States Food and Drug Administration (*FDA*) Adverse Event Reporting System data through the first quarter of 2018: Reports for bullous disorders (*BD*) by drug name

Drug (class)	No.	Safety signal[5] for BD	Date of FDA approval
Nivolumab (PD-1)	99	Yes	December 22, 2014
Pembrolizumab (PD-1)	43	Yes	September 2, 2014
Atezolizumab (PD-L1)	7	Yes	May 18, 2016
Durvalumab (PD-L1)	4	Yes	May 1, 2017
Avelumab (PD-L1)	0	No	March 23, 2017

PD, Programmed cell death; *PD-L1*, programmed cell death ligand 1.

Table II. Calculation of the proportional reporting ratio (*PRR*)[5]*

2×2 Table		
	Drug of interest	All other drugs
Adverse event of interest	a	B
All other Adverse Events	c	D

The χ^2 is calculated as per standard statistical formula: [(observed-expected)^2/expected]. Yates correction is recommended. Using the PRR, a signal is detected if the number of co-occurrences is ≥3 and the PRR is ≥2 with an associated χ^2 value of ≥4 or more.[5]
*PRR = [a/(a + c)]/[b/(b + d)].

used for detection of a safety signal. The PRR corresponds to the ratio of observed frequency (occurrence of the adverse event[s] of interest) in the exposed population (drug[s] of interest) to the nonexposed population (Table II). The PRR is a measure of association and may be considered by some to be the equivalent of the relative risk used for cohort studies. A safety signal is detected if the following criteria are met: number of events >3, χ^2 >4, and PRR >2.[5]

A safety signal was detected in FAERS for PD-1 inhibitors: nivolumab (n = 99; PRR, 5.87; 95% confidence interval [CI], 4.88-7.29), pembrolizumab (n = 43; PRR, 6.36; 95% CI, 4.71-8.59), and for 2 of 3 PD-L1 inhibitors: atezolizumab (n = 7; PRR, 3.31; 95% CI, 1.58-6.95) and durvalumab (n = 4; PRR, 7.87; 95% CI, 2.96-20.96). Although there were no reports for BDs with avelumab, this finding may or may not indicate there is a lower risk for BDs with avelumab. Importantly, for all agents, these findings do not indicate causality and cannot be used to determine incidence or risk ratio.[5]

A limitation for this study includes reporting bias within a voluntary reporting system such as FAERS along with possible report redundancy. Also, the retrospective nature of this study precludes medical record review and verification of previously collected data.

This postmarketing real-world data analysis revealed an association between BDs and exposure to a PD-1/PD-L1 inhibitor, in aggregate. Given that additional data are emerging for BDs and PD-1/PD-L1 inhibitors, these current findings from the FAERS database serve to further inform practitioners of newly evolving information about the risk for BDs associated with these agents.

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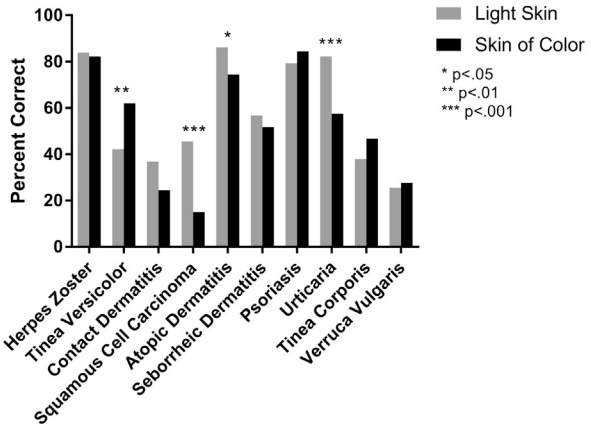

Fig 1. Percentage correct by skin condition, stratified by Fitzpatrick skin phototype.

Medical students' ability to diagnose common dermatologic conditions in skin of color

To the Editor: Dermatologic health care disparities disproportionately affect patients with skin of color (SoC) (defined as Fitzpatrick skin phototypes IV-VI), resulting in delayed treatment courses and increased morbidity and mortality.[1-3] Although many factors contribute to health care disparities, a lack of familiarity with disease presentation in patients with SoC is a physician-dependent factor that influences care quality.[1,2,4,5] The aim of this study was to assess medical students' diagnostic accuracy using clinical images of SoC and light skin (Fitzpatrick phototypes I-III).

Medical students at Tulane University School of Medicine and the University of Oklahoma College of Medicine were offered participation in a 10-item multiple choice quiz consisting of photos with a limited vignette without mention of race. Participants were randomly assigned to receive quiz A or B. Each quiz tested the same 10 conditions in the same order. Quiz A used photos from patients with Fitzpatrick I-III skin phototypes for odd-numbered questions and Fitzpatrick IV-VI skin phototypes for even-numbered questions; quiz B was the reverse.

A total of 227 students enrolled in the study (N = 227/1420; 16% response rate), 177 completed the study (n = 177/227, 78% completion rate). Preclinical medical students (years 1 and 2) scored an average of 47.3% on both quizzes compared with clinical medical students (years 3 and 4), who scored an average of 62.0% (t(175) = -5.51, $P < .00001$). Both medical schools include didactic lectures in dermatology during the preclinical years and offer elective clinical rotations.

Across all Fitzpatrick skin phototypes, the conditions most frequently identified correctly were herpes zoster (83.1%), psoriasis (81.9%), and atopic dermatitis (80.2%). The conditions least frequently identified correctly were verruca vulgaris (26.6%), contact dermatitis (30.5%), and squamous cell carcinoma (30.5%).

The conditions with the greatest disparity in visual diagnosis based on Fitzpatrick skin phototypes (Fitzpatrick IV-VI vs Fitzpatrick I-III) were squamous cell carcinoma (14.9% vs 45.6%, respectively; $t(175) = 4.662$; $P < .0001$), urticaria (57.5% vs 82.2%, respectively; $t(175) = 3.712$; $P = .0003$), and atopic dermatitis (74.4% vs 86.2%, respectively; $t(175) = -1.975$; $P = .0495$) (Fig 1). Nearly 34% of students misdiagnosed squamous cell carcinoma in SoC as melanoma, which may be explained by the students' reliance on dark pigment alone as the feature of melanoma. Students were more likely to correctly identify tinea versicolor in patients with SoC compared with patients with lighter skin phototypes (62.1% correct vs 42.2%, respectively; $t(175) = -2.681$; $P = .0082$) (Fig 1). The increase in diagnostic accuracy for tinea versicolor likely involves the prominent pigmentary change in SoC. Although not all statistically significant, 3 of the 4 diseases more accurately diagnosed in SOC were infections such as tinea corporis and verruca vulgaris. The study was limited by an overall low response rate and the fact that each participant did not serve as his/her own control.

Our study showed that medical students were less accurate in diagnosing squamous cell carcinoma, atopic dermatitis, and urticaria in patients with SoC but were more accurate in diagnosing tinea versicolor in SoC. These findings highlight the need to present all dermatologic conditions in both light skin and SoC as part of a comprehensive dermatology curriculum.

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