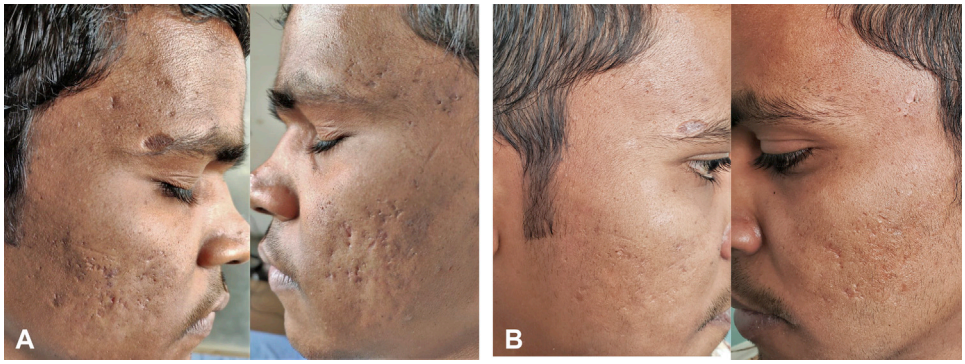

Fig 1. A, Multiple postacne atrophic scars on both sides of the face. **B,** Significant improvement on both sides of the face after microneedling with topical insulin (*right side*) and microneedling with platelet-rich plasma (*left side*).

In a mature PAS, type I collagen predominates more than type III.[1] After microneedling, collagen is deposited in the normal lattice pattern, while growth factors of PRP augment the healing of PAS.[2,3] TI activates of phosphatidyl inositol 3-kinase (PI3K)/protein kinase B (Akt) pathways to increase vascular endothelial growth factor.[4] After TI, increased synthesis and maturation of collagen fibers, chiefly type III, occurs in a basket weave-like organization (normal skin) rather than in a crisscross manner (scar).[5] Thus, PRP or insulin with microneedling augments the improvement in PAS.

The small sample size, lack of a separate assessment of each treatment modality, and short-term follow-up are limitations of our study. Use of a sophisticated vehicle for optimal delivery of insulin is desirable.

TI and PRP, combined with microneedling, may both achieve improvement, with an advantageous safety profile in PAS of skin-of-color populations. However, ready accessibility, low cost, and the noninvasive nature merits the use of TI over PRP. Further studies with a large sample size with histologic evaluations are needed to substantiate the efficacy of TI in PAS.

Authors want to thank the study participants and residents and head of the Department of Dermatology, Dr Vasantrao Pawar Medical College & Hospital & Research Centre, Nashik, India, for their kind cooperation in the study.

Manoj Pawar, MD,[a] and Mehak Singh, MD[b]

Department of Dermatology, Nashik District Maratha Vidya Prasarak Samaj Medical College, Nashik, Maharashtra[a]; and the Department of Dermatology, JK Medical College & Lok Nayak Hospital, Bhopal, Madhya Pradesh, India.[b]

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: This study received ethical approval from the Dr. Vasantrao Pawar Medical College, Hospital & Research Center.

Reprints not available from the authors.

Correspondence to: Manoj Pawar, MD, Flat No.11, Manomay Apartment, Savatanagar CIDCO, Nashik-422 008, Maharashtra State, India

E-mail: manojpawar624@yahoo.com

REFERENCES

1. Goodman GJ. Postacne scarring: a review of its pathophysiology and treatment. *Dermatol Surg*. 2000;26(9):857-871. https://doi.org/10.1046/j.1524-4725.2000.99232.x.
2. Cohen BE, Elbuluk N. Microneedling in skin of color: a review of uses and efficacy. *J Am Acad Dermatol*. 2016;74(2):348-355. https://doi.org/10.1016/j.jaad.2015.09.024.
3. Hesseler MJ, Shyam N. Platelet-rich plasma and its utility in the treatment of acne scars: a systematic review. *J Am Acad Dermatol*. 2019;80(6):1730-1745. https://doi.org/10.1016/j.jaad.2018.11.029.
4. AbdelKader DH, Osman MA, Elgizawy SA, et al. The role of insulin in wound healing process: mechanism of action and pharmaceutical applications. *J Anal Pharm Res*. 2016;2(1):7-10.
5. Azevedo F, Pessoa A, Moreira G, et al. Effect of topical insulin on second-degree burns in diabetic rats. *Biol Res Nurs*. 2016;18(2):181-192. https://doi.org/10.1177/1099800415592175.

https://doi.org/10.1016/j.jaad.2020.05.152

Utilization of immunotherapy among patients with stage 4 melanoma: An analysis of the National Cancer Database from 2012 to 2016

To the Editor: Immunotherapy offers unprecedented chances of sustained remission in stage 4 melanoma.[1] However, because of cutaneous adverse

Table I. Demographics of patients with stage 4 melanoma who did or did not receive immunotherapy as a first-line systemic treatment

Variable	Other systemic	Immunotherapy*	Effect size†	*P* value
All cases, n (%)	3932 (65.4)	2081 (34.6)		
Age, y				
Mean (SD)	67.9 (12.6)	64.6 (11.5)	0.274	<.001
Median	68	65		
Sex, n (%)				
Male	2715 (69.0)	1435 (69.0)	0.001	.942
Female	1217 (31.0)	646 (31.0)		
Race, n (%)				
White, non-Hispanic	3746 (95.3)	1978 (95.1)	0.005	.706
Other	186 (4.7)	103 (4.9)		
Charlson-Deyo score, n (%)				
0	2761 (70.2)	1618 (77.8)	0.081	<.001
1	770 (19.6)	303 (14.6)		
≥2	401 (10.2)	160 (7.7)		
Insurance, n (%)				
Private	1270 (32.3)	869 (41.8)	0.097	<.001
Uninsured	171 (4.3)	60 (2.9)		
Medicaid	258 (6.6)	112 (5.4)		
Medicare	2160 (54.9)	1003 (48.2)		
Other government insurance‡	73 (1.9)	37 (1.8)		
Facility, n (%)				
Academic	1539 (39.1)	1102 (53.0)	0.137	<.001
Community	1543 (39.2)	619 (29.7)		
Comp community§	341 (8.7)	116 (5.6)		
Integrated network	509 (12.9)	244 (11.7)		
Income quartile, n (%)‖				
Less than $40,227	607 (15.4)	239 (11.5)	0.070	<.001
$40,227-$50,353	907 (23.1)	425 (20.4)		
$50,354-$63,332	975 (24.8)	550 (26.4)		
$63,333+	1443 (36.7)	867 (41.7)		
US geographic region, n (%)				
Northeast	761 (19.4)	481 (23.1)	0.063	.003
Midwest	927 (23.6)	521 (25.0)		
Southeast	1543 (39.2)	692 (33.3)		
West	701 (17.8)	387 (18.6)		
Year of diagnosis, n (%)				
2012	763 (19.4)	162 (7.8)	0.243	<.001
2013	798 (20.3)	282 (13.6)		
2014	832 (21.2)	338 (16.2)		
2015	770 (19.6)	525 (25.2)		
2016	769 (19.6)	774 (37.2)		

SD, Standard deviation.

*There are 21 immunotherapy drugs associated with melanoma in the Surveillance Epidemiology, and End Result (SEER) Program medication database. Only 6 are approved by the US Food and Drug Administration for melanoma (interleukin 2, interferon alfa 2b, ipilimumab, nivolumab, pembrolizumab, and talimogene laherparepvec). The remaining are current or former clinical trial drugs/vaccines.

†Represents Cohen *D*, phi, or Cramer *V*.

‡Other government insurance.

§Comprehensive community cancer program.

‖Median household income of the patient's home zip code.

events,[2] dermatologists often comanage patients receiving immunotherapy with oncologists. Given the important role dermatologists play, it is helpful to understand how frequently immunotherapy is used in stage 4 melanoma and which patients are most likely to receive it. To investigate this, data from the National Cancer Database (NCDB) from 2012 through 2016 were analyzed.[3]

Table II. Logistic regression model for immunotherapy as the first systemic agent in stage 4 melanoma*

Variable	Univariate (95% CI)	*P* value	Multivariate (95% CI)	*P* value
Age	0.98 (0.97-0.98)	<.001	0.97 (0.97-0.98)	<.001
Charlson-Deyo Score				
0	1		1	
1	0.67 (0.58-0.78)	<.001	0.75 (0.65-0.88)	<.001
≥2	0.68 (0.56-0.83)	<.001	0.75 (0.61-0.92)	.005
Insurance				
Private	1		1	
Uninsured	0.51 (0.38-0.70)	<.001	0.64 (0.47-0.88)	.006
Medicaid	0.63 (0.50-0.81)	<.001	0.61 (0.47-0.78)	<.001
Medicare	0.68 (0.61-0.76)	<.001	1.10 (0.94-1.29)	.241
Other government insurance†	0.74 (0.49-1.11)	.146	1.00 (0.65-1.54)	.995
Facility				
Academic	1		1	
Community	0.56 (0.50-0.63)	<.001	0.59 (0.52-0.67)	<.001
Comp community‡	0.48 (0.38-0.60)	<.001	0.49 (0.38-0.62)	<.001
Integrated network	0.67 (0.56-0.79)	<.001	0.71 (0.59-0.85)	<.001
Income quartile§				
Less than $40,227	1		1	
$40,227-$50,353	1.19 (0.99-1.44)	.071	1.123 (0.92-1.37)	.256
$50,354-$63,332	1.43 (1.19-1.72)	<.001	1.36 (1.12-1.65)	.002
$63,333+	1.53 (1.29-1.81)	<.001	1.36 (1.12-1.64)	.002
US geographic region				
Northeast	1		1	
Midwest	0.89 (0.76-1.04)	.142	0.94 (0.79-1.11)	.463
Southeast	0.71 (0.61-0.82)	<.001	0.81 (0.69-0.95)	.009
West	0.87 (0.74-1.03)	.116	0.98 (0.81-1.17)	.797
Year of diagnosis				
2012	1		1	
2013	1.66 (1.34-2.07)	<.001	1.58 (1.26-1.97)	<.001
2014	1.91 (1.55-2.36)	<.001	1.97 (1.59-2.44)	<.001
2015	3.21 (2.62-3.93)	<.001	3.28 (2.67-4.03)	<.001
2016	4.74 (3.89-5.77)	<.001	5.06 (4.13-6.19)	<.001

CI, Confidence interval.
*Multicollinearity was not detected. A stepwise likelihood ratio test was performed; only covariates that increased goodness of fit were included in the final model.
†Other government insurance.
‡Comprehensive community cancer program.
§Median household income of the patient's home zip code.

The NCDB is a joint project of the American College of Surgeons and American Cancer Society. Neither organization is responsible for the conclusions of this study. Inclusion criteria were stage 4 melanoma and use of a systemic treatment. NCDB uses the Surveillance, Epidemiology, and End Results (SEER) Program medication database, which categorizes systemic treatments as chemotherapy (including BRAF and MEK inhibitors), hormonal therapy (used in hormone-responsive malignancies), or immunotherapy (PD-1/CTLA-4 inhibitors, interleukin 2, and interferon alfa).[4] The NCDB provides hospital facility data only for individuals 40 years and older. Thus, the analysis was limited to individuals 40 years and older. Individuals with missing demographic data were excluded (n = 561). To assess functional status, the Charlson-Deyo score was used, where an increasing score represents more comorbidities.

Descriptive statistics between individuals who did or did not receive immunotherapy were compared. A logistic regression model was subsequently constructed to identify factors associated with immunotherapy use. All analyses were completed in SPSS (IBM, Armonk, NY).

Among patients with stage 4 melanoma, 34.6% received immunotherapy as their first systemic treatment (Table I). Immunotherapy was more

common in individuals with a lower Charlson-Deyo score ($P < .001$), private insurance ($P < .001$), treatment at an academic facility ($P < .001$), and younger individuals ($P < .001$). The percentage of patients receiving immunotherapy rapidly increased from 17.5% in 2012 to 50.2% in 2016 ($P < .001$). Notably, no difference by sex ($P = .942$) or race/ethnicity ($P = .706$) was detected.

In the multivariate regression model, immunotherapy use was associated with diagnosis after 2012, particularly 2015 (odds ratio [OR], 3.28; 95% confidence interval [CI], 2.67-4.02), $P < .001$) and 2016 (OR, 5.06; 95% CI, 4.13-6.19; $P < .001$) and residing in zip codes with the third-highest (OR, 1.36; 95% CI, 1.12-1.65; $P = .002$) or highest (OR, 1.36; 95% CI, 1.12-1.64; $P = .002$) income quartile (Table II). Factors with less frequent immunotherapy use included older age (OR, 0.97; 95% CI, 0.97-0.98; $P < .001$), residing in the southeastern United States (OR, 0.81; 95% CI, 0.69-0.95; $P = .009$); and being uninsured (OR, 0.64; 95% CI, 0.47-0.99; $P = .006$) or having Medicaid insurance status (OR, 0.61; 95% CI, 0.47-0.78; $P < .001$).

These data show that between 2012 and 2016, there has been an explosive increase in the use of immunotherapy. This is likely due to the timing of US Food and Drug Administration approvals for ipilimumab (2011) and nivolumab (2014).[5] Although the data are limited up to 2016, we suspect an increasing trend may continue with future data. Overall, immunotherapy use is greater in younger, healthier, and more affluent individuals and is lower in older individuals, individuals with comorbidities, and those receiving care at nonacademic centers.

NCDB limitations include that data are available only through 2016, as well as lack of specificity regarding an exact immunotherapy given or tumor genetics.

Although oncologists prescribe immunotherapy, dermatologists are invaluable in diagnosing and managing its cutaneous adverse events. Together, both specialties deal with the benefits and adverse effects of these new treatments. As more patients with stage 4 melanoma receive immunotherapy, dermatologists should prepare themselves to manage and discuss these adverse events with both patients and oncologists.

Parth V. Shah, BA,[a] Jennifer N. Choi, MD,[a] Lori Fiessinger, MD,[b] Beatrice Nardone, MD, PhD,[a] Cuong V. Nguyen, MD,[a] and Walter Liszewski, MD[a,c]

From the Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois[a]; Department of Dermatology, University of Minnesota, Minneapolis, Minnesota[b]; and Division of Cancer Epidemiology, Northwestern University, Chicago, Illinois.[c]

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Not applicable.

Reprints not available from the authors.

Correspondence to: Walter Liszewski, MD, 676 N St. Clair St, Suite 1600, Chicago, IL 60610

E-mail: wjliszewski@gmail.com

REFERENCES

1. Bomar L, Senithilnathan A, Ahn C. Systemic therapies for advanced melanoma. *Dermatol Clin*. 2019;37:409-423.
2. Hwang SJ, Carlos G, Wakade D, et al. Cutaneous adverse events (AEs) of anti-programmed cell death (PD)-1 therapy in patients with metastatic melanoma: a single-institution cohort. *J Am Acad Dermatol*. 2016;74:455-461.e1.
3. American College of Surgeons. National Cancer Database, 1996-2020. Accessed April 18, 2020. Available at: https://www.facs.org/quality-programs/cancer/ncdb
4. National Cancer Institute. Drugs approved for melanoma. Accessed April 18, 2020. Available at: https://www.cancer.gov/about-cancer/treatment/drugs/melanoma; 2019.
5. Herrscher H, Robert C. Immune checkpoint inhibitors in melanoma in the metastatic, neoadjuvant, and adjuvant setting. *Curr Opin Oncol*. 2020;32:106-113.

https://doi.org/10.1016/j.jaad.2020.06.031

Dynamic cytokine profiles combined with enzyme-linked immunospot assay are useful for immunologically confirming the dapsone hypersensitivity syndrome

To the Editor: Dapsone hypersensitivity syndrome (DHS) is a dapsone-induced T−cell mediated delayed type of hypersensitivity, characterized by fever, rash, lymphadenopathy, and hepatic function abnormalities.[1] The diagnosis of DHS is traditionally based on the criteria proposed by Richardus and Smith.[1] However, the diagnosis remains a challenge in clinical practice due to the difficulty of distinguishing DHS from other drug-induced hypersensitivity reactions (DHRs), concurrent infections, or other underlying diseases. The enzyme-linked immunospot (ELISpot) method quantifying the release of antigen-specific cell cytokines has been widely used in diagnosis of DHR by distinguishing culprit drugs from coadministered drugs.[2]