but she appeared healthy, with no evidence of MiTES, suggesting a normal upper limit of 15 repeats. All MiTES patients investigated to date were homozygous (18/18) or compound heterozygous (17/18). Two HSAN8 families had polyalanine tract expansion,[3] a Pakistani family homozygous for 19 repeats and an Irish family showing unusually mild disease, MiTES-type lesions, and homozygosity for 18 repeats. The evidence thus suggests that 17 or 18 repeats produces the localized MiTES phenotype, whereas 19 or more causes HSAN8. Polyalanine expansions are a known cause of genetic disease, previously described in 9 genes, 8 of which, like *PRDM12*, encode transcription factors associated with congenital syndromes.[5]

In summary, we have increased the number of reported cases of MiTES to 13, reported resolution of excoriations with persistent scarring in an adult, confirmed the cause as biallelic polyalanine expansions in *PRDM12* to 17 or 18 repeats, and revised the normal upper limit of repeats to 15.

We gratefully acknowledge the help of our clinical colleagues: Drs L. Taylor, E.T. Ooi, K. McWilliams, and the late Olivia Schofield at Edinburgh Royal Infirmary, and Drs D. Parsad and S. Dogra at Post Graduate Institute of Medical Education & Research, Chandigarh.

Arun C. Inamadar, FRCP,[a] Keshavmurthy Vinay, MRCP,[b] Bayanne Olabi, MRCP,[c] Nivedita Sarveswaran, MSc,[d] Anuradha Bishnoi, MD,[b] Christopher G. Woods, PhD,[d,e] and Celia Moss, FRCP[f,g]

From the Department of Dermatology, Shri BM Patil Medical College & Hospital, BLDE (Deemed to be University), Bijapur,[a] and Department of Dermatology, Post Graduate Institute of Medical Education & Research, Chandigarh,[b] India; the Department of Dermatology, Edinburgh Royal Infirmary,[c] the Cambridge Institute for Medical Research,[d] the Department of Medical Genetics, University of Cambridge,[e] Department of Dermatology, Birmingham Children's Hospital,[f] and College of Medical and Dental Sciences, University of Birmingham,[g] United Kingdom

Prior presentation: Patients 1 and 2 were presented by Prof Inamadar at the 31st Annual Society for Pediatric Dermatology Pre-AAD meeting, Washington, DC, February 28-March 1, 2019. Patient 5 was presented by Dr Olabi at the British Society for Paediatric Dermatology Annual Meeting, Glasgow, Scotland, November 9-10, 2018.

Funding: Supported by Biotechnology and Biological Sciences Research Council CASE studentship Ref BB/N504142/1 to Nivedita Sarveswaran and by National Institute of Health Biomedical Centre award to Cambridge 2017-2022, Integrated genomics theme, ref RG85443 to Dr Woods.

Conflicts of interest: None disclosed.

Reprint requests: Celia Moss, FRCP, Department of Dermatology, Birmingham Children's Hospital, Steelhouse Ln, Birmingham B4 6NH, UK

E-mail: celia.moss@nhs.net

REFERENCES

1. Srinivas SM, Vykuntaraju KG, Owen CM, Moss C, Hiremagalore R. Mid-face toddler excoriation syndrome (MiTES): a new paediatric diagnosis. *Clin Exp Dermatol*. 2017;42(1):68-71.
2. Moss C, Srinivas SM, Sarveswaran N, et al. Midface toddler excoriation syndrome (MiTES) can be caused by autosomal recessive biallelic mutations in a gene for congenital insensitivity to pain, PRDM12. *Br J Dermatol*. 2018;179(5):1135-1140.
3. Chen Y-C, Auer-Grumbach M, Matsukawa S, et al. Transcriptional regulator *PRDM12* is essential for human pain perception. *Nat Genet*. 2015;47(7):803-808.
4. Oaklander AL. Neuropathic itch. *Semin Cutan Med Surg*. 2011; 30(2):87-92.
5. Hughes JN, Thomas PQ. Molecular pathology of polyalanine expansion disorders: new perspectives from mouse models. In: Hatters DM, Hannan AJ, eds. *Tandem Repeats in Genes, Proteins, and Disease*. Totowa, NJ: Humana Press; 2013:135-151.

https://doi.org/10.1016/j.jaad.2019.05.036

Retrospective cohort study of anatomic localization of cutaneous squamous cell carcinomas in solid organ transplant recipients compared with immunocompetent patients

To the Editor: Solid organ transplant recipients (SOTRs) are at 65- to 250-fold increased risk of developing cutaneous squamous cell carcinoma (SCC). Their SCCs may behave more aggressively than SCCs in immunocompetent individuals.[1] As a potential reason for this observed difference in clinical outcomes, we asked whether the anatomic distribution of SCCs in SOTRs significantly differed compared with immunocompetent patients.

We conducted a retrospective cohort study of the anatomic location of primary SCCs in adult SOTRs and immunocompetent patients of the Yale Transplant Dermatology Clinic between January 1, 2008, and December 31, 2015. This study was approved by the Yale University Institutional Review Board. Data on age, sex, race, immunosuppression, and anatomic site of histopathologically confirmed SCCs sorted into 5 regions were collected.

Table I. Comparison of anatomic location of tumors in the study population

	SOTR		Immunocompetent				
Location	No. (%)[†]	Patients, No.	No. (%)[†]	Patients, No.	RR*	95% CI	*P*
Head and neck[‡]	67 (40.1)	32	24 (21.6)	15	1.90	1.04-3.47	.038[§]
Ear and lip	16 (9.6)	12	8 (7.2)	5	1.38	0.42-4.56	.598
Trunk	14 (8.4)	10	21 (18.9)	15	0.46	0.21-1.03	.059
Upper extremities	51 (30.5)	21	27 (24.3)	15	1.28	0.57-2.86	.552
Lower extremities	19 (11.4)	10	31 (27.9)	12	0.42	0.14-1.24	.118

CI, Confidence interval; *RR*, relative risk; *SOTR*, solid organ transplant recipient.
*SOTR vs immunocompetent.
[†]Number of squamous cell carcinomas (% total squamous cell carcinomas in group).
[‡]Except high-risk ear and lip region.
[§]Highlights a significant association.

Age- and sex-adjusted negative binomial regression with robust sandwich estimator was used to account for tumor count data overdispersion. The generalized estimating equation method was used to compare tumor location between groups while taking correlation between multiple tumors from the same patient into account. Significance level was $P < .05$, two-sided. Negative binomial regression and generalized estimating equation contrast estimates were done using SAS 9.4 software (SAS Institute Inc, Cary, NC).

We included 58 SOTRs and 40 immunocompetent patients. In these same cohorts, we previously found that sex and race were not significantly different between groups and that the immunocompetent patients were older than SOTRs (73.4 vs 65.0 years, $P < .001$).[2] There were no significant differences in the risk of developing an SCC observed in the ear and lip region or on the upper extremities between the groups (Table I). The risk of developing an SCC in the head and neck was observed to be 90% greater in SOTRs than in immunocompetent patients (relative risk [RR], 1.90; 95% confidence interval [CI], 1.04-3.47). The difference in risk of developing SCC in the trunk region (RR, 0.46; 95% CI, 0.21-1.03) and the lower extremities (RR, 0.42; 95% CI, 0.14-1.24) trended toward significance between the 2 groups.

The increased risk of developing SCCs on the head and neck in SOTRs may reflect their increased susceptibility to ultraviolet-induced carcinomas. Although not statistically significant, the increased risk of ear and lip (RR, 1.38) and upper extremities (RR, 1.28) regions in SOTRs may further reinforce this hypothesis because these areas are commonly chronically sun exposed. The trend toward decreased risk of developing SCCs on the lower extremities may be due to these sites being prone to a distinct set of indolent squamous proliferations, which have features of SCCs but can regress with conservative treatment such as steroids.[3,4]

Criteria for high-risk SCCs include tumor diameters >2 cm, higher histologic grade, subcutaneous tissue invasion, and location in the scalp, eyelids, ears, nose, or lips, or a combination of these. The high-risk SCCs that develop on the head and neck may partially explain worse outcomes in SOTRs.

In a previous study, male SOTRs developed more SCCs on their head and neck compared with female SOTRs.[5] To our knowledge, our study is the first to show that SOTRs are at significantly increased risk for developing their SCCs on the head and neck compared with an immunocompetent population. Vigilant surveillance, including the head and neck of SOTRs by transplant teams and dermatologists, may lead to improved clinical outcomes.

Joyce Y. Cheng, MD, MHS,[a] Fang-Yong Li, MPH, MS,[b] Mike Wang, BS,[a] and Oscar R. Colegio, MD, PhD[a,c,d,e,f]

From the Department of Dermatology,[a] Yale Center for Analytical Sciences,[b] Departments of Pathology[c] and Surgery,[d] Yale Cancer Center,[e] and Yale Transplant Dermatology Clinic at the Yale New Haven Transplantation Center;[f] Yale University School of Medicine, New Haven, Connecticut.

Dr Colegio is currently affiliated with the Department of Dermatology and is Professor of Oncology, Roswell Park Comprehensive Cancer Center.

Funding sources: This study was supported by the National Institutes of Health, National Center for Advancing Translational Sciences Clinical Translational Science Award Program TL1. The funding sponsor was not involved in the design and conduct of the study, collection, management, analysis, and interpretation of data,

preparation, review, or approval of the manuscript, or the decision to submit the manuscript for publication.

Conflicts of interest: None disclosed.

Reprints not available from the authors.

Correspondence to: Oscar R. Colegio, MD, PhD, Department of Dermatology and Professor of Oncology, Roswell Park Comprehensive Cancer Center, Elm and Carlton Streets, Buffalo, New York 14263.

E-mail: oscar.colegio@roswellpark.org

REFERENCES

1. Gonzalez JL, Reddy ND, Cunningham K, Silverman R, Madan E, Nguyen BM. Multiple cutaneous squamous cell carcinoma in immunosuppressed vs immunocompetent patients. *JAMA Dermatol*. 2019;155:625-627.
2. Cheng JY, Li FY, Ko CJ, Colegio OR. Cutaneous squamous cell carcinomas in solid organ transplant recipients compared with immunocompetent patients. *JAMA Dermatol*. 2018;154:60-66.
3. Ko CJ, Glusac EJ, McNiff JM, Rodic N, Leffell DJ. Squamous proliferations on the legs of women: qualitative examination of histopathology, TP53 sequencing, and implications for diagnosis in a series of 30 cases. *J Am Acad Dermatol*. 2017;77:1126-1132.e1.
4. Sanders S, Busam KJ, Halpern AC, Nehal KS. Intralesional corticosteroid treatment of multiple eruptive keratoacanthomas: case report and review of a controversial therapy. *Dermatol Surg*. 2002;28:954-958.
5. Lindelof B, Dal H, Wolk K, Malmborg N. Cutaneous squamous cell carcinoma in organ transplant recipients: a study of the Swedish cohort with regard to tumor site. *Arch Dermatol*. 2005;141:447-451.

https://doi.org/10.1016/j.jaad.2019.05.054

Analysis of conflicts of interest in pharmaceutical payments made to Food and Drug Administration physician advisers after dermatologic drug approval

To the Editor: Academic physicians have regularly served as voting members of advisory committees for the United States Food and Drug Administration (FDA).[1-3] These committee members serve as external experts to the FDA in determining whether a new medical therapy is fit for the United States market.[2,3] Considering that financial conflicts of interest have been shown to impact member voting habits, physician financial ties have been a topic of ongoing discussion.[2-5] A recent study found that many former FDA advisors receive large sums of money from pharmaceutical companies once their advisory role is complete.[3] Some fear these relationships may incentivize future committee members to expect after-the-fact rewards for favorable voting habits.[3] The FDA has guidelines to minimize financial conflicts of interest but does not make stipulations about postadvisory role financial relationships.[3]

Investigations using publicly available Open Payment data from the Centers for Medicare and Medicaid Services database have analyzed post hoc advisory role payments to physician advisors in the approval of psychopharmacologic, rheumatologic, cardiac, and renal drugs.[2] To our knowledge, these analyses have not been reported for dermatologic drug advisors. The purpose of this study was to review Open Payment data for industry payments made to former dermatologic drug committee members.

Payments made to United States physicians who advised FDA committees during the approval of 8 dermatologic therapies were analyzed using the Open Payment database. Drugs were chosen from recently approved dermatology medications from CenterWatch.com and included those used frequently and infrequently by dermatologists: brodalumab, dalbavancin, deoxycholic acid, dupilumab, peginterferon alfa-2b, secukinumab, tedizolid phosphate, and ustekinumab.[3] Data were collected from 2013 to 2017. This range was selected because no data are available before 2013, and 2017 correlated with the most recent data available.[4] Payments classified as general payments were recorded and included consulting fees, speaking fees, educational expenses, food and beverage expenses, and travel and lodging expenses.

Of the 61 physician advisers, 33 (54%) received at least 1 industry payment after dermatologic drug approval. Of the 33 receiving 1 payment, 9 (27%) accepted more than $1000, 6 (18%) accepted more than $10,000, 5 (15%) accepted more than $50,000, and 3 (9%) accepted more than $100,000. The 33 physician advisers received a mean ± standard deviation of $47,860.62 ± $85,938. The standard deviation was larger than the mean due to the nonnormal distribution of the data. For the drugs examined, payments from competing pharmaceutical companies outnumbered payments from the drug manufacturer (Table I).

Our research concludes former FDA committee advisors for dermatologic drugs frequently received payments from industry. Furthermore, a significant proportion (24%) of those who accepted payments received funds in excess of $50,000. Critics of such industry–physician relationships argue these payments could incentivize FDA advisors to alter their voting habits.[3] Others conclude post hoc industry payments should not be discouraged