

spent on a small number of patients (<1%) who require expensive systemic therapy. A limitation of this study is that claims data rely on the accuracy of coding by physicians. Medicare data include information only on individuals age 65 year and older; therefore, additional studies that include patients of all ages are needed to generate a comprehensive analysis of skin cancer spending.

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#### **Survey analysis on the management of moderately dysplastic nevi among academic dermatologists across the United States**



*To the Editor:* Currently there are no clinical guidelines for the management of moderately dysplastic nevi (DN), and the decision to observe, rebiopsy, or excise remains up to the discretion of the dermatologist. Many dermatopathologists do not embrace the

grading system of mild, moderate, or severe dysplasia but simply comment on the presence of architectural or cytologic atypia. In the literature to date, there is significant variation and lack of consensus on the management of moderate DN,<sup>1-3</sup> the histologic criteria, and the use of the term moderate DN. In fact, low interobserver reproducibility in the classification of dysplastic nevi between dermatopathologists viewing the same lesion, demonstrated by low kappa values in both experienced and less experienced dermatopathologists, has been demonstrated previously.<sup>4</sup> The purpose of this study was to better understand the management of biopsy-proven moderate DN among academic dermatologists, given their critical role in influencing the future practice guidelines of dermatology.

After University of South Florida Institutional Review Board approval was obtained, an anonymous survey of 12 multiple-choice questions was e-mailed to the 385 members of the Association of Professors of Dermatology. Respondents were asked to indicate how they would manage biopsy-proven moderate DN in 9 different situations, selecting from 5 different management options (Tables I and II).

A total of 131 (34%) members (52 programs) of the Association of Professors of Dermatology listserv completed the survey, with 12 respondents indicating that their institution did not use the term moderate DN. We found notable variability in the management of biopsy-proven moderate DN among academic dermatologists (Tables I and II). The only scenario with high concordance was in the management of moderately DN with clear biopsy margins and without visible pigment, with 93% (124) of respondents choosing clinical monitoring. However, 5% of respondents still chose surgical excision with 2–3-mm margins, highlighting the lack of consensus.

Our results show varied management depending on biopsy margin and residual pigment status; however, certain trends can be recognized. In all scenarios with a positive biopsy margin, the majority of respondents chose a second procedure over clinical monitoring (Table II), irrespective of pigment at the biopsy site. Both repeat biopsy and excision at various margins are done with the intent to obtain a histologically clear margin; however, each subcategorization of these procedures can be used to reflect the comfort level of practitioners with moderate DN.

The absence of visible pigment in a positive biopsy margin (lateral, deep, deep and lateral) markedly increased the percentage of respondents who chose clinical monitoring (45%, 40%, 37%, respectively). Surgical excision (2–3-mm margin)

**Table I.** Response rates for management of biopsy-proven moderate dysplastic nevi

Type of biopsy-proven moderate dysplastic nevi	Clinical monitoring, % (n)	Rebiopsy with wider, deeper margin, % (n)	Surgical excision with 2–3-mm margin, % (n)	Surgical excision with 4-mm margin, % (n)	Surgical excision with >5-mm margin, % (n)	Total
Clear margins without visible pigment	93.23 (124)	1.50 (2)	5.26 (7)	0 (0)	0 (0)	133
Clear margins with visible pigment at base	29.77 (39)	40.46 (53)	28.24 (37)	1.53 (2)	0 (0)	131
Clear margins with visible pigment at periphery	29.77 (39)	35.88 (47)	31.30 (41)	1.53 (2)	1.53 (2)	131
Deep margins without visible pigment	40.46 (53)	27.48 (36)	29.01 (38)	0.76 (1)	2.29 (3)	131
Deep margins with visible pigment	19.08 (25)	35.11 (46)	42.75 (56)	0.76 (1)	2.29 (3)	131
Lateral margins without visible pigment	45.04 (59)	28.24 (37)	22.14 (29)	2.29 (3)	2.29 (3)	131
Lateral margins with visible pigment	21.37 (28)	39.69 (52)	35.11 (46)	1.53 (2)	2.29 (3)	131
Deep and lateral margins without visible pigment	37.40 (49)	26.72 (35)	30.53 (40)	3.05 (4)	2.29 (3)	131
Deep and lateral margins with visible pigment	16.29 (22)	31.20 (41)	48.09 (63)	1.53 (2)	2.29 (3)	131

**Table II.** Response rates comparing clinical monitoring and all procedure types

Type of biopsy-proven moderate dysplastic nevi	Clinical monitoring, % (n)	All procedural interventions,* % (n)
Clear margins without visible pigment	93.2 (124)	6.8 (9)
Clear margins with visible pigment at base	29.8 (39)	70.2 (92)
Clear margins with visible pigment at periphery	29.8 (39)	70.2 (92)
Deep margins without visible pigment	40.5 (53)	59.5 (78)
Deep margins with visible pigment	19.1 (25)	80.9 (106)
Lateral margins without visible pigment	45.0 (59)	55.0 (72)
Lateral margins with visible pigment	21.4 (28)	78.6 (103)
Deep and lateral margins without visible pigment	37.4 (49)	62.6 (82)
Deep and lateral margins with visible pigment	16.3 (22)	83.7 (109)

\*All procedural interventions included rebiopsy and surgical excision of any margin length.

was chosen over rebiopsy when deep biopsy margins were positive, regardless of residual pigment or peripheral margin involvement. The only scenarios in which respondents chose rebiopsy over surgical excision were clear biopsy margin with visible pigment (peripheral and deep) and positive lateral biopsy margin, regardless of pigmentation status.

A recent consensus statement from the Pigmented Lesion Subcommittee of the Melanoma Prevention Working Group, which reviewed several studies on the clinical management of moderate DN, concluded that incompletely excised moderate DN without pigment could be observed and not re-excised.<sup>5</sup> Interestingly, while the Pigmented Lesion Subcommittee favors clinical monitoring for moderate DN, our study shows that academic dermatologists continue to rebiopsy or excise this type of moderate DN.

This study highlights that there are significant variances in the management of moderate DN among academic dermatologists and that previously

published consensus guidelines have not been broadly adopted.

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### Dupilumab use in allergic contact dermatitis



*To the Editor:* Dupilumab is an interleukin 4 (IL-4) receptor  $\alpha$  (IL-4R $\alpha$ ) inhibitor indicated in recalcitrant moderate-to-severe atopic dermatitis (AD).<sup>1</sup> Although contact dermatitis is considered a helper T-cell 1 (T<sub>H</sub>1 cell)—mediated process, certain allergens sensitize by induction of T<sub>H</sub>2 pathways.<sup>2</sup> Our retrospective case-study suggests that dupilumab might be effective in the inhibition of weaker allergens that elicit a T<sub>H</sub>2-mediated IL-4—dependent allergic contact dermatitis (ACD).

A retrospective chart review was performed to identify all patients treated with dupilumab for recalcitrant dermatitis by 2 dermatologists at their respective clinical sites (Center for Dermatology, PA, Florham Park, New Jersey, and Loma Linda Veterans Hospital, Loma Linda, California). Clinical evaluations had been performed by the respective dermatologist as part of the clinical management, using a modified physician global assessment. All patients had been assessed for body surface area (BSA) involvement, severity index, and itch at baseline and 10-12 weeks after starting dupilumab. The patients continued to receive clinical care on an as

needed basis thereafter. No side effects were associated with dupilumab. Table 1 (available at <http://www.jaad.org>) depicts demographic and clinical information, including areas involved, patch-test proven allergen sensitivities, previous failed systemic therapies, and treatment outcomes of all 15 patients.

The majority of these adult patients had a history of childhood AD and current hand dermatitis (73%). Recalcitrant facial dermatitis was prevalent during the dupilumab treatment in a significant number of the cases. The percent BSA affected by dermatitis ranged 10%-80% (mean 48%), and the percent improvement after dupilumab ranged 70%-100% (mean 85%). A weak-negative ( $R = -0.1181$ ,  $R^2 = 0.0139$ ) correlation with patient age and weak-positive correlation with BSA ( $R = 0.06$ ,  $R^2 = 0.0038$ ) were associated with improvement on dupilumab. In all, the 15 patients had sensitivities to 46 distinct allergens. The most frequent clinically relevant allergens were cocamidopropyl betaine (CAPB) (40%), nickel (33%), oleamidopropyl dimethylamine (27%), *Myroxylon pereirae* (20%), and fragrance mix 1 (20%).

Most of these adult patients had AD, a predominant T<sub>H</sub>2-axis immune disorder. It has been reported that inflamed atopic skin is predisposed to the development of T<sub>H</sub>2-mediated contact sensitization to weaker potency allergens, such as fragrances, emulsifiers, and surfactants (eg, CAPB).<sup>2,3</sup> Of note, a recent report by Puza and Atwater described a patient who elicited a 1+ patch reaction to the potent sensitizer methylisothiazolinone rather than an indeterminate (+/-) reaction to the weaker allergen dimethylaminopropylamine (a precursor of CAPB) while on dupilumab for severe AD.<sup>4</sup> The role of IL-4 in ACD has been demonstrated by IL-4—knockout mice, which still have the ability to elicit contact sensitivities to oxazolone but not 2,4,6-trinitrochlorobenzene, a contact allergen with T<sub>H</sub>2-mediated sensitization.<sup>5</sup>

Prevalent nickel sensitization was expected given the hapten's ubiquity and atopic hand dermatitis association.<sup>2</sup> However, the attenuation of nickel dermatitis was unanticipated and notably suggests that nickel sensitization can involve the elicitation of the T<sub>H</sub>2/IL-4 pathway. The remarkable clinical and quality-of-life improvements achieved by this group of prior frequent flyer patients mirrors the dramatic impact of biologics on psoriasis. This study highlights the untapped potential of IL-4 inhibitors in the treatment of adult patients with a history of AD and recalcitrant and systematized ACD to certain allergens.<sup>2</sup>

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