RESEARCH LETTERS

Dermatologist Preferences for Treatments to Compare in Future Randomized Controlled Comparative Effectiveness Trials for Moderate to Severe Psoriasis

Approximately 1.2 million Americans have moderate to severe psoriasis, a chronic, inflammatory disease of the skin and joints that has substantial impact on health-related quality of life and is associated with excess cardiovascular risk and mortality.[1] Despite the rapid growth of treatments for psoriasis, insufficient data exist to distinguish between first- and second-line therapies. Thus, as emphasized by the Institute of Medicine,[2] there exists a critical need for comparative effectiveness research (CER) in psoriasis treatment. Since a crucial component of CER is to identify the priorities of stakeholders such as physicians, we conducted a study to describe US dermatologists' preferences for which treatments to compare in future randomized controlled trials (RCTs) in moderate to severe psoriasis.

Methods. We surveyed 1000 US dermatologists (500 National Psoriasis Foundation [NPF] members and 500 American Academy of Dermatology [AAD] members who self-reported that they treat psoriasis) as part of a larger study on preferences for psoriasis therapy. Dermatologists were asked to select 3 treatments they would most like to compare in an RCT for moderate to severe psoriasis from a list of 10 US Food and Drug Administration (FDA)–approved biological and oral systemic treatments and phototherapies (**Figure 1**). The order of treatment listings was randomized in 6 ways to reduce bias. Detailed data on the survey methods have been published elsewhere.[3,4] The study was approved by the University of Pennsylvania institutional review board and conducted from May to August 2010.

The primary outcome was dermatologists' preferences for treatments to compare in an RCT, as indicated by each treatment's cumulative frequency of first, second, or third choice selection. Preferences were summarized descriptively and compared with respect to major provider characteristics.

Results. We received questionnaire responses from 387 dermatologists (39% response rate). Responding dermatologists were mostly male (72%), NPF members (64%), and private practitioners (70%). Respondents were similar to nonrespondents with respect to sex, duration of practice, and geographic region. Additional data on respondents' baseline characteristics have been previously described.[4] Of note, respondents indicated that a median of 90% of their patients with psoriasis being treated with systemic medications or phototherapy also concurrently used topical agents by prescription.

The treatments dermatologists most wanted to compare in an RCT were etanercept (58.7% [95% CI, 53.6%-63.6%]), adalimumab (50.9% [95% CI, 45.8%-56.0%]), ustekinumab (50.1% [95% CI, 45.0%-55.2%]), and methotrexate (45.5% [95% CI, 40.4%-50.6%]) (**Figure 2**). When preferences were stratified by provider characteristics, including sex, NPF vs AAD membership, geographic region, duration of practice, prac-

1. Which three treatments would you most like to see compared in a randomized controlled trial for moderate-to-severe psoriasis?

Please rank your top three choices by filling in one circle in each column below:

Treatment	1st Choice (choose one)	2nd Choice (choose one)	3rd Choice (choose one)
Phototherapy (PUVA)	○	○	○
Phototherapy (UV-B)	○	○	○
Acitretin	○	○	○
Cyclosporine	○	○	○
Methotrexate	○	○	○
Adalimumab	○	○	○
Alefacept	○	○	○
Etanercept	○	○	○
Infliximab	○	○	○
Ustekinumab	○	○	○
Other (Please specify):	○	○	○

Figure 1. Questionnaire item assessing dermatologists' preferences for treatments to include in future trials. Note that treatment options were randomized in 6 different orders to reduce bias. PUVA indicates psoralen plus UV-A.

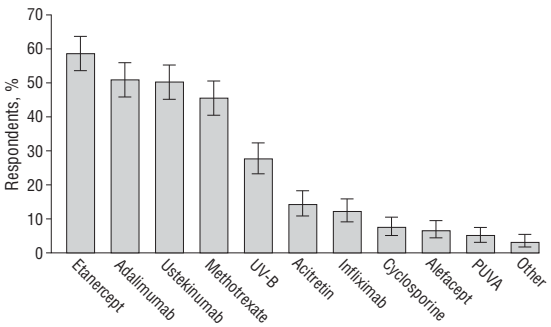

Figure 2. Preferences for treatments to compare in a randomized controlled trial. Error bars indicate 95% CIs. PUVA indicates psoralen plus UV-A.

©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/19/2013

tice type, patient volume, and infusion center affiliation, the top 4 overall treatments remained the same, although the order of treatments within the top 4 occasionally differed. The presence of phototherapy units in the practice affected the degree of preference for including UV-B phototherapy in CER trials: 34.1% (95% CI, 28.3%-40.3%) of dermatologists with phototherapy units vs 14.6% (95% CI, 8.9%-22.1%) of dermatologists without phototherapy units selected UV-B therapy. However, the top 4 overall treatments were the same regardless of phototherapy availability.

Comment. Our results indicate that US dermatologists who treat psoriasis prefer to compare the newer subcutaneously administered tumor necrosis factor inhibitors and interleukin-12/23 inhibitor and the traditional oral systemic methotrexate in future CER trials. Etanercept, adalimumab, and ustekinumab gained FDA approval for plaque psoriasis in 2004, 2008, and 2009, respectively. Methotrexate, however, has been widely used since its approval in 1972.

Notably, our research group[4] had previously observed that UV-B was the most preferred first-line treatment by dermatologists who treat psoriasis, followed by etanercept, adalimumab, and methotrexate, while UV-B was only the fifth most requested treatment for RCT inclusion among these providers. Ustekinumab, on the other hand, was the third most requested treatment to include in CER trials but was ranked as only the sixth most preferred first-line treatment for moderate to severe psoriasis.[4]

Our results also indicate that the concurrent use of prescription topical agents with systemic or phototherapy is common, but most RCTs have prohibited combination therapy.[5] Thus, for CER trials to reflect real-world practice, permitting the concomitant use of topical prescription therapy should be considered.

Our findings are highly informative for future trial design because they represent the priorities of hundreds of US dermatologists who actively treat patients with psoriasis. Future studies should examine the priorities of other stakeholders, such as payers and patients, and other elements of CER trial design, such as primary efficacy outcomes, safety end points on which to discriminate, and treatment duration.

Joy Wan, BA
Katrina Abuabara, MD, MA
Andrea B. Troxel, ScD
Daniel B. Shin, BA
Abby S. Van Voorhees, MD
Bruce F. Bebo Jr, PhD
Gerald G. Krueger, MD
Kristina Callis Duffin, MD
Joel M. Gelfand, MD, MSCE

Accepted for Publication: August 21, 2011.
Author Affiliations: Department of Dermatology (Ms Wan, Drs Abuabara, Van Voorhees, and Gelfand, and Mr Shin), Center for Clinical Epidemiology and Biostatistics (Drs Troxel and Gelfand), and Department of Biostatistics and Epidemiology (Drs Troxel and Gelfand and Mr Shin), University of Pennsylvania Perelman School of Medicine, Philadelphia; National Psoriasis Foundation, Portland, Oregon (Dr Bebo); Department of Dermatology, University of Utah School of Medicine, Salt Lake City, Utah (Drs Krueger and Callis Duffin).
Correspondence: Dr Gelfand, 1471 Penn Tower, One Convention Ave, Philadelphia, PA, 19104 (joel.gelfand@uphs.upenn.edu).
Author Contributions: Ms Wan and Dr Gelfand had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Abuabara, Van Voorhees, Bebo, Krueger, Callis Duffin, and Gelfand. *Acquisition of data:* Abuabara, Shin, Krueger, and Gelfand. *Analysis and interpretation of data:* Wan, Troxel, Shin, and Gelfand. *Drafting of the manuscript:* Wan. *Critical revision of the manuscript for important intellectual content:* Wan, Abuabara, Troxel, Shin, Van Voorhees, Bebo, Krueger, Callis Duffin, and Gelfand. *Statistical analysis:* Wan, Troxel, Shin, and Gelfand. *Obtained funding:* Krueger and Gelfand. *Administrative, technical, and material support:* Wan, Abuabara, Shin, Bebo, Krueger, and Gelfand. *Study supervision:* Gelfand.
Financial Disclosure: Dr Van Voorhees served on the advisory board of and was an investigator and speaker for Amgen and Genentech, receiving honoraria and grants; she was a consultant for Incyte, Leo, VGX, and Xtrac, receiving honoraria; she served on the advisory board and was a speaker for Abbott, Centocor, and Connetics, receiving honoraria; she served on the advisory board and was an investigator for Bristol-Myers Squibb and Warner Chilcott, receiving honoraria and grants; she was an investigator for Astellas, IDEC, and Roche, receiving grants; she served as a consultant for Amgen; and she received honoraria from Synta. Dr Bebo has had relationships with Abbott, Amgen, Astellas, Centocor, Galderma, Genentech, PhotoMedix, Stiefel/GSK, Warner Chilcott, and Wyeth, receiving other benefits. Dr Krueger served on the steering committees for Centocor/Phoenix 2 and Golimumab/psoriatic arthritis, receiving no compensation; he served on the steering committee for PSOLAR, receiving other financial benefit; he served on the data monitoring board for Novartis and as chair of the data-monitoring safety board for Pfizer, receiving other financial benefit; was a consultant and/or advisory board member for Abbott, Almirall, Amgen, Anacor, Astellas, Boehringer Ingelheim, Bristol-Myers Squibb, Centocor, CombinatoRx, Genzyme, Isis, Lilly, L'Oreal, Lupin Limited, MedaCorp, Medicis, Novartis, Novo Nordisk, Pfizer, Schering-Plough, Somagenics, theDerm.org, Synvista, Warner Chilcott, UCB, Vascular Biogenics Limited, and ZARS, receiving honoraria or other financial benefit; he was a stockholder in ZARS, receiving stock options; he was a speaker for Abbott, Amgen, Astellas, Centocor, and the National Psoriasis Foundation, receiving honoraria; and he was an investigator for Abbott, Amgen, and Centocor, receiving grants. Dr Callis Duffin was an investigator, consultant, and speaker for Abbott, Amgen, and Centocor, receiving honoraria and salary; she served on the advisory board of Amgen; and received residency/fellowship program funding from Abbott and Amgen. Dr Gelfand served as consultant and

©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/19/2013

investigator with Abbott, Amgen, Centocor, Genentech, Novartis, and Pfizer, receiving grants and honoraria; he was a consultant with Celgene, Covance, Galderma, Shire Pharmaceuticals, and Wyeth, receiving honoraria; and he was an investigator with Shionogi, receiving grants.

Funding/Support: This study was supported by grant RC1-AR058204 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (Dr Gelfand), Training Grant T32-AR07465 from the National Institutes of Health (Ms Wan and Mr Shin), and the Doris Duke Clinical Research Fellowship (Dr Abuabara).

Role of the Sponsors: The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of data; or in the preparation, review, or approval of the manuscript.

1. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. *JAMA*. 2006;296(14):1735-1741.
2. Sox HC, Greenfield S. Comparative effectiveness research: a report from the Institute of Medicine. *Ann Intern Med*. 2009;151(3):203-205.
3. Wan J, Abuabara K, Shin DB, Troxel AB, Bebo BF Jr, Gelfand JM. Dermatologist response rates to a mailed questionnaire: a randomized trial of monetary incentives. *J Am Acad Dermatol*. 2012;66(1):e18-e20.
4. Wan J, Abuabara K, Troxel AB, et al. Dermatologist preferences for first-line therapy of moderate to severe psoriasis in healthy adult patients [published online August 18, 2011]. *J Am Acad Dermatol*. 10.1016/j.jaad.2011.03.012.
5. Naldi L, Svensson A, Zenoni D, et al; European Dermato-Epidemiology Network. Comparators, study duration, outcome measures and sponsorship in therapeutic trials of psoriasis: update of the EDEN Psoriasis Survey 2001-2006. *Br J Dermatol*. 2010;162(2):384-389.

Online First

Impact of Guidance From a Computer-Aided Multispectral Digital Skin Lesion Analysis Device on Decision to Biopsy Lesions Clinically Suggestive of Melanoma

A major challenge faced daily by clinical dermatologists is to determine which pigmented lesions are appropriate for biopsy. The present study was designed to determine the effect of guidance provided by a multispectral digital skin lesion analysis (MSDSLA) device (MelaFind; MELA Sciences Inc)[1] on dermatologists' decision to biopsy a pigmented lesion and the impact of the information provided by the device on the associated melanoma biopsy sensitivity and specificity. MelaFind uses light from visible to near-infrared wavelengths to image up to 2.5 mm beneath the skin and analyzes images from subbands of these wavelengths to provide information about the lesion's level of structural disorder. The device provides an output of "positive" or "negative" as an additional piece of data that can be integrated into the biopsy decision.

Methods. A total of 179 practicing dermatologists (median duration of practice, 11-15 years) attending an educational conference participated in an interactive melanoma session. Participants were asked to evaluate 24 pigmented lesions (5 melanomas and 19 other pigmented lesions) that had been analyzed as part of a prior study using a MSDSLA system.[2] To make the experience more clinically realistic, the lesions were grouped from 4 composite patients, each having 6 lesions, with matching historic and clinical characteristics. Patient histories were presented, and then distant and close-up clinical and dermoscopic images of each of the lesions were viewed.

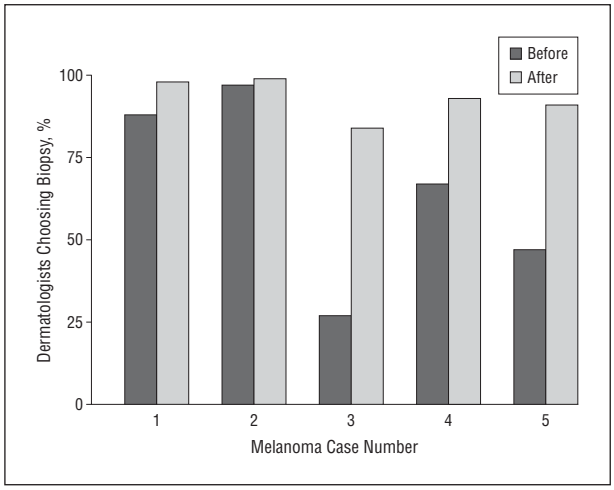

Figure 1. Percentage of study dermatologists who chose to biopsy melanomas before and after the receipt of the multispectral digital skin lesion analysis (MSDSLA) information. The overall biopsy choice of 69% before receipt of the MSDSLA information improved to 94% after information receipt.

Each dermatologist responded yes or no on an electronic keypad to the following question: "Would you biopsy this lesion?" Then, the MSDSLA system information was provided, and the participant responded to this question: "Would you now biopsy this lesion?" Individual responses before and after MSDSLA information were compared to determine the effect of the MSDSLA information on the biopsy decision. The study was deemed exempt by the institutional review board of New York University.

Results. For 179 dermatologists, the MSDSLA information improved the average biopsy sensitivity for the 5 melanomas from 69% prior to receiving the MSDSLA information to 94% after receiving the information ($P < .001$) (**Figure 1**). Biopsy specificity declined from 54% before to 40% after MSDSLA information receipt ($P < .001$). Biopsy rates of lesions that were MSDSLA negative fell from 43% before to 25% after MSDSLA information receipt ($P < .01$). Of the 4 lesions that were not evaluable by the MSDSLA system, biopsy rates went from 37% before to 42% after the dermatologists learned that no MSDSLA information would be available ($P = .16$, showing neither a positive nor negative effect when the system provided no additional information).

Integration of the MSDSLA data into the biopsy decision process also led to a more uniform decision by the dermatologists. The multirater κ statistic for interobserver agreement improved from 0.32 before to 0.45 (fair to moderate) after receipt of the additional information provided from the MSDSLA system.

The changes in biopsy decisions made as a result of integrating the MSDSLA device increased the overall biopsy sensitivity with a concomitant lesser decrease in over-

©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/19/2013