Dermatologist preferences for treatments to compare in future randomized controlled comparative effectiveness trials for moderate-to-severe psoriasis

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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, there exists a critical need for comparative effectiveness research (CER) in psoriasis treatment.[2] Since a crucial component of CER is to identify the priorities of stakeholders such as physicians, we conducted a study to describe U.S. dermatologists' preferences for which treatments to compare in future randomized controlled trials (RCTs) in moderate-to-severe psoriasis.

Methods

We surveyed 1000 U.S. 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 three treatments they would most like to compare in a RCT for moderate-to-severe psoriasis from a list of 10 Food and Drug Administration (FDA)-approved biologic, oral systemic, 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 Penn Institutional Review Board and conducted from May to August 2010.

The primary outcome was dermatologists' preferences for treatments to compare in a 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 (39.1% response rate). Responding dermatologists were mostly male (72%), NPF members (64%), and private practitioners (70%). Respondents were similar to non-respondents 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 psoriasis patients on systemic medications or phototherapy also concurrently used topicals by prescription.

The treatments dermatologists most wanted to compare in a RCT were etanercept (59%; 95% confidence interval (CI) 53.6–63.6%), adalimumab (51%; 95% CI 45.8–56.0%), ustekinumab (50%; 95% CI 45.0–55.2%), and methotrexate (45%; 95% CI 40.4–50.6%) (Figure 2). When preferences were stratified by provider characteristics, including sex, NPF versus AAD membership, region, duration of practice, practice type, patient volume, and infusion center affiliation, the top four overall treatments remained the same although the order of treatments within the top four occasionally differed. The presence of phototherapy units in the practice affected the degree of preference for including ultraviolet (UV) B phototherapy in CER trials [34.1% (95% CI 28.3–40.3%) versus 14.6% (95% CI 8.9–22.1%) of dermatologists without units selected UVB]; however, the top 4 overall treatments were the same regardless of phototherapy availability.

Comment

Our results indicate that U.S. 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, we had previously observed that UVB was the most-preferred first-line treatment by dermatologists who treat psoriasis followed by etanercept, adalimumab, and methotrexate;[4] however, UVB 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 topicals with systemic or phototherapy is common; however, most previous RCTs have prohibited combination therapy.[5] Thus, in order 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 as they represent the priorities of hundreds of U.S. 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 endpoints upon which to discriminate, and treatment duration.

Acknowledgments

References

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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 (UVB)	○	○	○
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: treatment options were randomized in 6 different orders to reduce bias).
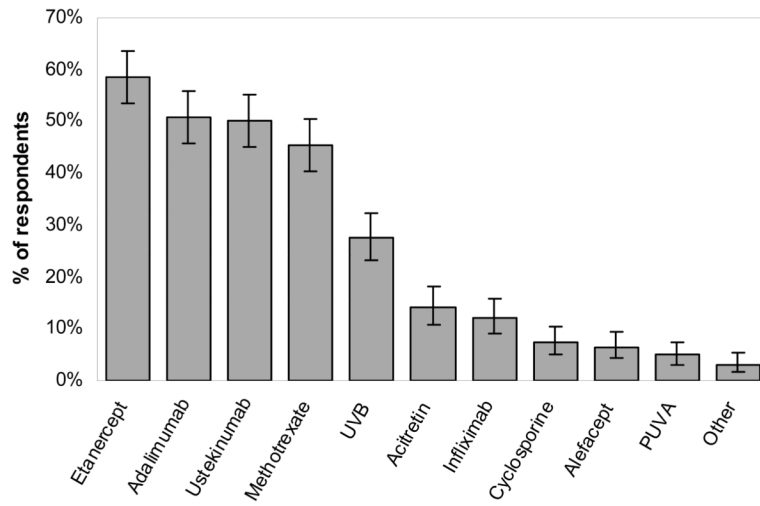
FIGURE 2. Preferences for treatments to compare in a randomized controlled trial
Error bars indicate 95% confidence interval.