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BRIEF REPORT

Reassurance Techniques Do Not Significantly Impact Confidence in Biosimilars for Psoriasis: A Survey of a Convenience Sample of Individuals with Self-Identified Psoriasis

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ABSTRACT

Introduction: Biosimilars are underutilized, and negative perceptions may hinder their acceptance by patients. Psychologic interventions have not been extensively studied in the context of alleviating biosimilar hesitancy. The objective of this study was to assess the effectiveness of psychologic interventions on biosimilar confidence.

Methods: Following institutional review board (IRB) approval, 1285 subjects with self-reported psoriasis were recruited using Amazon Mechanical Turk, an online crowdsourcing platform. Participants were randomized to one of ten groups. Group A started with a hypothetical bio-originator; group B started with a hypothetical biosimilar. The remaining groups were provided a hypothetical scenario in which they were switching to a biosimilar after achieving great results with a bio-originator, and were randomized to receive either no reassurance (group C) or one of the following psychologic interventions: reassurance of comparable effectiveness (group D), an illustration implying comparable effectiveness (group E), anecdote of great results obtained in "other psoriasis patients" (group F), anecdote of great results obtained in another psoriasis patient "a lot like you" (group G), reassurance of the rigorous evaluation process to gain Food and Drug Administration (FDA) approval (group H), engagement in a task designed to facilitate recognition of biosimilars' comparability through answering multiple choice (group I) or free response questions (group J). Confidence levels were assessed using six-point Likert scales and analyzed using one-way analysis of variance (ANOVA) and two-group *t*-tests.

Results: While no statistically significant differences were detected, illustrations implying comparability (mean 4.19), explanations of the rigorous process to gain FDA approval (mean 4.21), testimonials of treatment success in another psoriasis patient "a lot like you" (mean 4.07) and "other psoriasis patients" (mean 4.01),

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and engagement with multiple choice (mean 4.02) and free response answers (mean 4.08) improved biosimilar confidence compared with the biosimilar switch control group (mean 3.96).
Conclusion: Identifying highly impactful methods of improving biosimilar confidence remains a challenge.

Keywords: Access; Biosimilars; Confidence; Psoriasis; Treatment

Key Summary Points

While biosimilars have promising potential to benefit both patients and the entire healthcare system, skepticism has hindered their acceptance by patients.

Psychologic interventions can increase patient willingness to initiate biological treatment, thus we hypothesized that presenting illustrations implying comparability to bio-originators, sharing testimonials, explaining the approval process, and engaging subjects in mental tasks designed to facilitate recognition of biosimilars' comparability would improve perceptions of biosimilars.

Illustrations implying comparable effectiveness, explanation of the rigorous approval process, testimonials, and engagement improved confidence in biosimilars; however, the differences were not statistically significant ($p > 0.05$).

Identifying interventions that meaningfully improve patient perceptions of biosimilars remains a challenge.

INTRODUCTION

While numerous biologic medications have been developed to treat psoriasis, access can be limited owing to their high costs [1]. Biosimilars were introduced to expand access to high-quality treatments, but they face barriers to adoption. Patients may have negative perceptions of cost-effective alternative drugs owing to a lack of knowledge [2, 3]. There is a need to educate patients on biosimilars' clinical equivalence to bio-originators, and specific interventions have not yet been extensively tested [4–6]. We sought to identify effective methods of increasing patient confidence in biosimilar drugs for the treatment of psoriasis.

METHODS

Upon obtaining Wake Forest School of Medicine Institutional Review Board approval, subjects were recruited through Amazon Mechanical Turk, an online crowdsourcing platform used extensively in psychosocial research [7]. Inclusion criteria for subjects included: having self-reported psoriasis, being at least 18 years of age, and having an Amazon Mechanical Turk account. Before participating, subjects were provided with a fact sheet summarizing the study's background, aims, and the details regarding their involvement. They were then directed to the survey (Table 1) on Qualtrics, a secure web-based survey platform. Upon completion of the survey, participants were compensated US $0.05.

Sociodemographic information, including: age, sex, race, ethnicity, education level, and annual household income, was collected. Participants were then randomized into one of ten survey groups in a 1:1:1:1:1:1:1:1:1:1 double-blind ratio using Qualtrics randomization (Table 1; Fig. 1). Two groups were provided a hypothetical scenario in which they were stepping up to biologic therapy from a topical corticosteroid cream; group A received a hypothetical brand-name biologic and group B received a hypothetical biosimilar. Groups C–J were provided a hypothetical scenario in which they were patients who achieved great results from a hypothetical brand-name biologic for the past two years and were being asked to switch to a hypothetical biosimilar. Participants were randomized to receive either no reassurance (group C) or one of the following psychologic interventions: informed of evidence of

Table 1 Survey script

Group A—Start on hypothetical bio-originator (biological naïve)

After discussing your personal treatment preferences, your doctor prescribes you to a brand-name biological product, Zoltava (rivezumab)

Group B—Start on a hypothetical biosimilar (biological naïve)

After discussing your personal treatment preferences, your doctor prescribes you to Truneeva (rivezumab), an FDA-approved biosimilar of Zoltava (rivezumab)

Group C—No reassurance (biosimilar switch)

After discussing the circumstances regarding your insurance, your doctor writes you a prescription for the biosimilar medication, Truneeva (rivezumab)

Group D—Mention "clinical evidence" of biosimilar achieving comparable results to bio-originator (biosimilar switch)

While writing your prescription, your physician mentions there is clinical evidence of Truneeva (rivezumab) achieving comparable results to the brand-name, Zoltava (rivezumab), in psoriasis patients

Group E—Present illustration depicting biosimilar achieving comparable results to bio-originator (biosimilar switch)

While writing your prescription, your physician mentions there is clinical evidence of Truneeva (rivezumab) achieving comparable results to the brand-name, Zoltava (rivezumab), in psoriasis patients. Your physician then hands you a figure of the results obtained (Fig. 2)

Group F—Testimonial with "other psoriasis patients" (biosimilar switch)

While writing your prescription, your physician mentions that he/she saw great results with Truneeva (rivezumab) in other psoriasis patients

Group G—Testimonial with "another psoriasis patient a lot like you" (biosimilar switch)

Table 1 continued

While writing your prescription, your physician mentions that he/she saw great results with Truneeva (rivezumab) in another psoriasis patient a lot like you

Group H—Highlight the rigorous evaluation process biosimilars go through for approval (biosimilar switch)

While writing your prescription, your physician mentions that Truneeva (rivezumab) has undergone rigorous evaluation to become an FDA-approved Zoltava (rivezumab) biosimilar and that comparative data have demonstrated both structural and functional biosimilarity of Truneeva (rivezumab) to Zoltava (rivezumab)

Group I—Explanation and engagement with multiple choice options (biosimilar switch)

After discussing the circumstances regarding your insurance, you ask your physician for more information about biologics/biosimilars. He/she responds with:

"Biologics are too difficult for any company to duplicate exact copies, so even two batches of a brand-name biologic from the same company will differ. However, the slight variability between batches or between a brand-name drug and a biosimilar drug does not cause meaningful differences in safety or potency"

Your physician then asks you: how would you explain this to another patient?

A. There are no real differences between the brand-name drug and the biosimilar

B. While there are minor differences between biosimilars and brand name drugs, the differences are not meaningful

C. While there are minor differences between biosimilars and brand name drugs, there are also differences between different batches of the brand names drugs, and those differences are not meaningful

Table 1 continued

D. While there are minor differences between biosimilars and brand name drugs, and differences between different batches of the brand names drugs, those differences do not affect efficacy or safety

E. Other

Group J—Explanation and engagement with free response (biosimilar switch)

After discussing the circumstances regarding your insurance, you ask your physician for more information about biologics/biosimilars. He/she responds with:

"Biologics are too difficult for any company to duplicate exact copies, so even two batches of a brand-name biologic from the same company will differ. However, the slight variability between batches or between a brand-name drug and a biosimilar drug does not cause meaningful differences in safety or potency"

Your physician then asks you: how would you explain this to another patient?

[free response]

How confident are you with your planned treatment?

1—Completely Not Confident

2—Mostly Not Confident

3—Somewhat Not Confident

4—Somewhat Confident

5—Mostly Confident

6—Completely Confident

comparable clinical effectiveness (group D), presented an illustration depicting comparable effectiveness (group E; Fig. 2), anecdotes of treatment success in "other psoriasis patients" (group F), anecdotes of treatment success in another psoriasis patient "a lot like them" (group G), an explanation of the rigorous evaluation biosimilars undergo to gain FDA approval (group H), or an explanation of biologics and biosimilars followed by a question asking them how they would explain it to another patient with multiple choice options (group I) or free response format (group J). Participants' confidence with their treatment plans were measured using six-point Likert scales (1—"completely not confident", 2—"mostly not confident", 3—"somewhat not confident", 4—"somewhat confident", 5—"mostly confident", 6—"completely confident"). Results were evaluated using one-way analysis of variance and two-group *t*-tests. p-values < 0.05 were considered significant.

RESULTS

Subjects with self-reported psoriasis ($n = 1285$) were recruited from 17 May 2020 to 25 January 2021. Most ($n = 1253$) subjects completed the survey (97.5% response rate). There were no significant differences between the groups' demographic characteristics ($p > 0.05$). Participants had a mean age of 36 years (standard deviation 11.9 years) and were slightly predominantly female (53%). Subjects were most commonly Caucasian (65%), African American (12%), and Asian/Pacific Islander (12%). The majority of participants held bachelor's degrees (51%) or higher (16%) and had annual household incomes over US $50,000 (53%).

With the exception of group D (mention of "clinical evidence" of biosimilar comparability, mean 3.81, standard deviation 1.26), each intervention produced slightly higher treatment confidence compared with the biosimilar switch control group (mean 3.96, standard deviation 1.12) ($p = 0.13$). The highest confidence scores were produced by presenting an illustration depicting biosimilar and biologic comparability (group E; mean 4.19, standard deviation 1.05) and explaining the rigorous evaluation biosimilars undergo to gain FDA approval (group H; mean 4.21, standard deviation 1.14) (Table 2). Testimonials of treatment success produced slightly greater increases in confidence when stating "another psoriasis patient a lot like you" (group G; mean 4.07, standard deviation 1.06) versus "other psoriasis

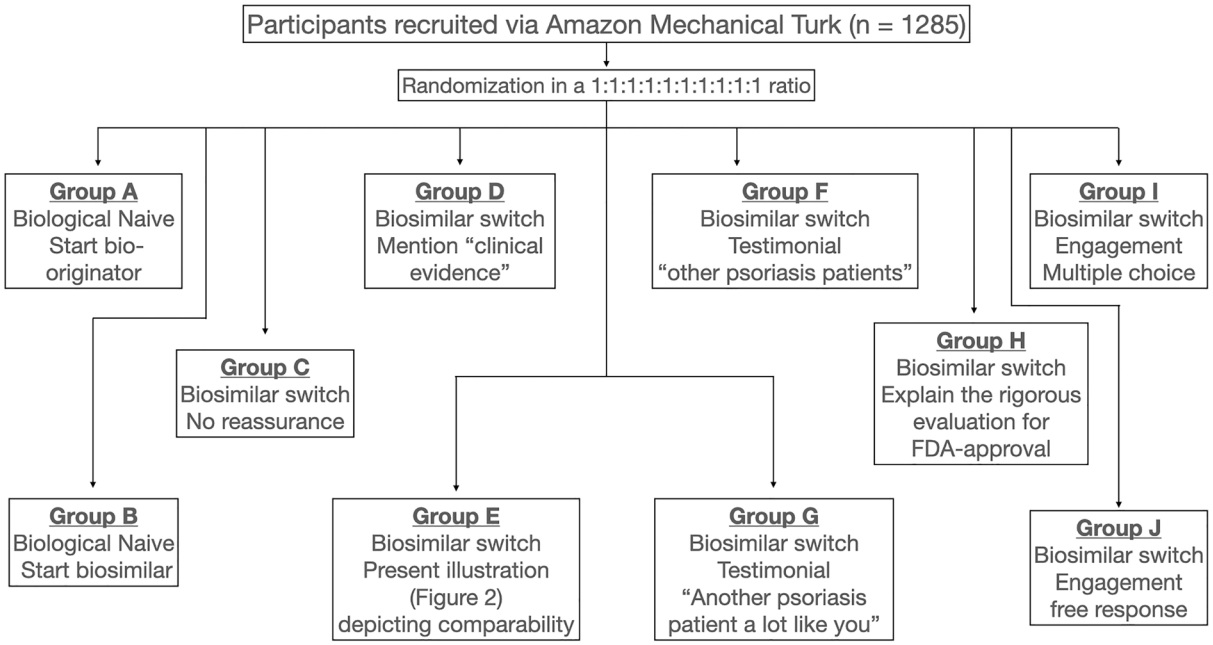

Fig. 1 Flow chart of hypothetical scenarios and interventions for each randomized group

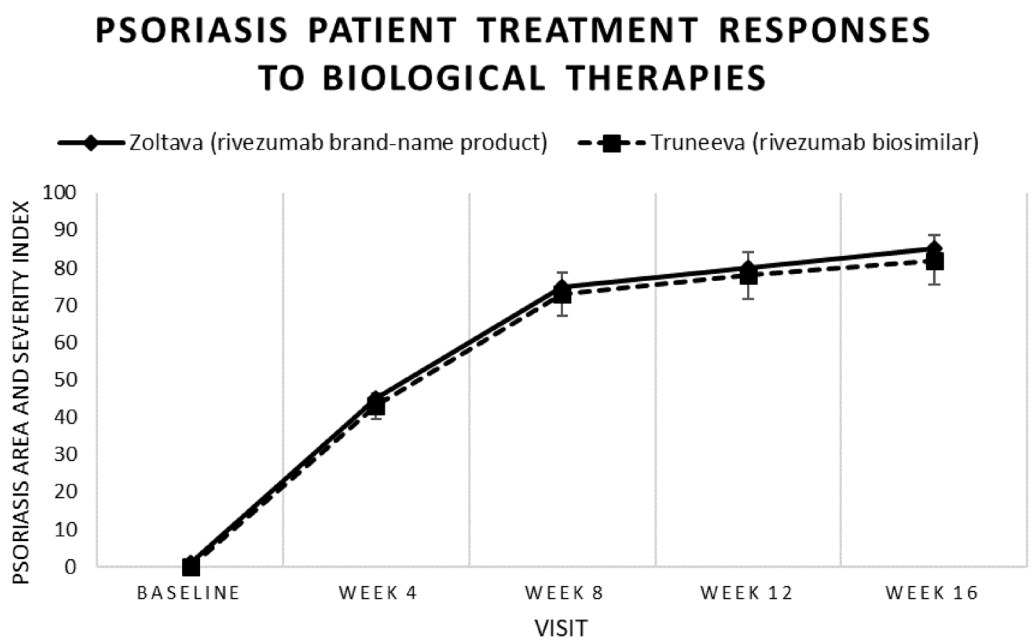

Fig. 2 Group E's intervention: an illustration depicting biosimilars' comparable effectiveness to a brand-name bio-originator

patients" (group F; mean 4.01, standard deviation 0.97). Engagement with free response (group J; mean 4.08, standard deviation 1.25) was slightly more effective at improving confidence than multiple choice options (group I; mean 4.02, standard deviation 1.21). Although the reassurance interventions generally produced small trends in the expected

Table 2 Confidence scores for each randomized group

Group	A	B	C	D	E	F	G	H	I	J
Mean	3.79	3.98	3.96	3.81	4.19	4.01	4.07	4.21	4.02	4.08
Standard deviation	1.33	1.03	1.12	1.26	1.05	0.97	1.06	1.14	1.21	1.25

direction, no statistically significant differences were detected.

DISCUSSION

Many of the psychologic interventions assessed in this study are easily implementable techniques that can be utilized by clinicians to improve dermatology patient outcomes. For example, presenting clinical evidence and providing anecdotes of treatment success can improve caregiver willingness to treat childhood atopic dermatitis with corticosteroids [8]. Engagement can increase willingness to initiate biologic treatment in psoriasis patients [9]. Improving confidence in biosimilar drugs is an important step toward expanding access to effective psoriasis medications. However, it does not appear biosimilar confidence is much improved by the psychologic interventions assessed in the present study nor by our previous study which involved positively framing them as the "gold" alternative to bio-originators [10].

This study has several limitations. Our quantitative approach did not allow for collection of qualitative concerns about biosimilars to guide the development of future interventions aimed at addressing patients' skepticism. Mechanical Turk is more effective at producing high quality data with short and simple experiments than with open-ended questions, thus descriptive results such as subjects' baseline knowledge of biosimilars and subjective concerns were not assessed [11]. It is unclear whether participants' responses reflect their true decisions as hypothetical cognitive-based scenarios may fail to accurately simulate real-world clinical situations. Mechanical Turk is primarily used in psychometric analysis to evaluate general trends and attitudes; its validity as a research tool in dermatology is not yet well established and its sample population may not be strongly representative of specific populations such as patients with psoriasis [12, 13]. While our sample had a higher proportion of racial minorities than may be typical of psoriasis cohorts, and participants were not clinically evaluated in person, subjects were asked to participate only if they had histories of psoriasis; our data collection occurred over an 8 month period which may reflect the time required to accumulate subjects who actually had psoriasis. Although it is possible that some participants did not truly carry formal diagnoses of psoriasis, disease-naive and/or treatment-naive individuals may have perspectives on biosimilars that are similar to patients who are not well attuned to their condition. Because we aimed to randomize participants across several interventions, generating a sample through alternative methods, such as using ICD-10 codes, may have precluded adequate sample size and/or a timely investigation. Convenience sampling through Mechanical Turk allowed for relatively quick and cost-effective data collection on a large scale.

Our recruitment methods are subject to inherent selection bias. Mechanical Turk users are typically more highly educated than the general population, and a considerable proportion (67.4%) of our sample held a bachelor's degree or higher [12]. Individuals with higher educational attainment may be more attuned to their conditions and might be better able to navigate the analysis of graphs than those with lower education levels. Another potential concern with Mechanical Turk's user base is the presence of highly active and experienced workers ("Super Turkers") who may be familiar with survey questions; their participation can compromise data quality from reduced responsiveness to experimental manipulations and/or inflation of measures of ability due to learning or practice effects [11, 12].

Despite the limitations associated with conducting survey studies through Mechanical Turk, it is a resource-efficient tool for feasibly conducting randomized controlled psychologic studies on a large scale and can generate results largely comparable with more conventional means of data collection [14]. We believe it can be a particularly useful and sufficiently valid method of detecting highly effective interventions that produce large differences; none of the interventions we tested appeared highly effective.

CONCLUSION

Although psychologic interventions can positively impact patient outcomes, the reassurance techniques assessed in this study do not appear to have a significant effect on confidence in biosimilars. Reiterating the rigorous evaluation process that biosimilars undergo to gain FDA approval and/or providing patients with illustrations depicting biosimilars' comparability to bio-originators appear to produce small improvements in biosimilar confidence and may be interventions to focus on for future development. While identifying highly effective simple strategies for improving perceptions of biosimilar drugs remains a challenge, negative findings can help influence the design of future experiments, reduce duplications of effort, and prevent randomly positive results from falsely appearing promising.

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Compliance with Ethics Guidelines. This study was reviewed and approved by the Wake Forest School of Medicine Institutional Review Board (#IRB00065491). Before participating, subjects were provided with a fact sheet summarizing the study's background, aims, and the details regarding their involvement. They were then directed to the survey (Table 1) on Qualtrics, a secure web-based survey platform.

Data Availability. All data generated or analyzed during this study are included in this published article and as supplementary material.

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