Rapid Response of Biologic Treatments of Moderate-to-Severe Plaque Psoriasis: A Comprehensive Investigation Using Bayesian and Frequentist Network Meta-analyses

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Video Abstract

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Abstract

Plaque psoriasis profoundly affects patients' quality of life, underscoring the need for timely and effective treatments. Although several biologics are available to treat psoriasis, determining the best treatment option is difficult, as head-to-head comparisons of biologics are rare. To address that gap, researchers analyzed studies involving adults with moderate-to-severe psoriasis treated with inhibitors of IL -17, IL-12/23, IL-23, or tumor necrosis factor. Thirty-three phase 3, double-blind, randomized, controlled trials were included in the analysis, which represented 11 biologics approved for the treatment of moderate-to-severe psoriasis in adults. This study focused on response rates in the first 12 weeks of treatment because rapid skin clearance and quality of life improvement are important patient preferences in biologic treatment. Outcome measures included improvements of at least 75, 90, and 100 percent in the Psoriasis Area and Severity Index, or PASI, at 2, 4, 8, and 12 weeks of treatment; and a score of 0 to 1 on the Dermatology Life Quality Index, or DLQI, at week 12, indicating no impact of psoriasis on quality of life. A Bayesian network meta-analysis enabled inclusion of head-to-head and placebo-controlled studies. That allowed for direct and indirect comparisons of treatment effects between populations and across many interventions. The average response to each treatment was calculated versus placebo and represented as a Himalayan plot. On a Himalayan plot, drugs with the greatest estimated treatment effect lie farthest along the x-axis. High, narrow curves indicate a high degree of certainty, whereas short, wide curves indicate less certainty. For example, curve A represents a drug with high certainty of an estimated low treatment effect. Compared with all other biologics, ixekizumab and brodalumab showed more rapid treatment effects on PASI75 response rates over weeks 2, 4, and 8; at week 12, ixekizumab and risankizumab had the most rapid treatment effects, with some overlap with other biologics. Similarly, ixekizumab and brodalumab showed more rapid treatment effects on PASI90 response rates over weeks 2, 4, 8, and 12, resulting in the highest PASI90 response rates; similar trends were observed in PASI100 response rates. Regarding quality of life, treatment effect on DLQI scores was greatest for ixekizumab, brodalumab, and secukinumab at week 12, with some overlap between these treatments. Several limitations of this NMA study should be noted, including, reliance on both direct and indirect comparisons, potential trial heterogeneity, imputation methods for missing data, exclusion of other important endpoints, and other notable limitations. Overall, these findings suggest that ixekizumab and brodalumab could provide the most rapid skin clearance and quality-of-life improvement versus other biologics for patients with moderate-to-severe psoriasis, including secukinumab, an IL-17 antagonist, and inhibitors of IL-12/-23, IL-23, or TNF pathways. That's important because rapid skin improvements and feeling noticeably better quickly are critical to psoriasis therapy and rank among the highest priorities for patients. Fast effects are also tied to longer-term outcomes, including skin improvement, quality of life, and reduction in itch. And considering individual patient needs along with physician goals may help improve adherence to and satisfaction with therapy for plaque psoriasis.