COMMENTARY

Emerging treatments for lupus nephritis: health equity considerations in clinical research and coverage

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Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that affects between 300,000 and 1.5 million people in the United States.¹ SLE disproportionately affects women and Black and Hispanic individuals.^{2,3} Specifically, the prevalence of SLE is 9 times higher among women than men, 4 times higher among Black individuals compared with White individuals, and 2 times higher among Hispanic compared with non-Hispanic adults. Approximately a third of patients with SLE develop kidney disease (lupus nephritis, LN),¹ and about 10%-20% of those with LN develop end-stage renal disease.^{4,5} Black patients with LN are 9 times more likely to develop end-stage renal disease than White individuals.^{6,7}

Before 2020, the standard therapy available to treat LN included high-dose corticosteroids in combination with mycophenolate mofetil or cyclophosphamide. In the past year, the US Food and Drug Administration approved an oral calcineurin inhibitor, voclosporin, and a B-lymphocyte inhibitor, belimumab, as add-ons to standard combination therapy for LN. The authorization of belimumab for LN was based on the findings from the BLISS-LN trial, which found that belimumab increased the odds of a primary efficacy renal response by 60% and of a complete renal response by 70%

when compared with standard therapy alone.⁸ The AURORA trials demonstrated that voclosporin doubled the odds of a complete renal response compared with standard therapy alone.⁹

The Institute for Clinical and Economic Review (ICER) recently reviewed the cost-effectiveness of these therapies.¹⁰ At current pricing (\$43,000 per year for belimumab and \$92,000 per year for voclosporin) ICER determined that both drugs are cost-effective according to the incremental cost-effectiveness ratios considered reasonable in the United States (\$150,000 per quality-adjusted life-year).¹⁰

However, the ICER report highlighted substantial uncertainty over the results for Black patients.¹⁰ Although LN disproportionately affects Black patients, Black study participants only accounted for 5%-14% (n=14-61) of the enrollees in the clinical trials that evaluated belimumab and voclosporin.^{8,9,11} Belimumab and voclosporin were associated with a significant renal response in the overall study population; however, the sample size available provided inadequate statistical power to detect a significant treatment effect in Black patients. Thus, it remains unknown whether the renal benefits of voclosporin and belimumab observed in

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clinical trials are generalizable to the Black population.

The low representation of non-White patients in clinical trials precludes the understanding of how critical social determinants, such as income, educational attainment, and neighborhood-level characteristics, influence treatment response. This is

important because previous studies have shown that social and structural factors contribute to variation in SLE and LN outcomes and therapy access.¹² For instance, previous work has shown that low-income SLE patients have to travel longer distances to see their rheumatologists and are more likely to have emergency room admissions for SLE complications.¹³

Race and ethnicity are social constructs, and social determinants of health are underlying factors that contribute towards racial/ethnic inequities.¹⁴ The absence of diversity in clinical study participation may sustain health inequities by failing to account for social and structural factors in the investigation of novel therapies.¹⁵

The potential for belimumab and voclosporin to sustain health inequities in LN care goes beyond clinical trial composition. Although ICER deemed belimumab and voclosporin cost-effective, the approval of these new agents presents affordability and access issues concerning their use.¹⁰ In order to not exceed ICER's budget impact threshold, only 80% and 30% of patients with LN eligible to receive belimumab and voclosporin, respectively, would receive these therapies.¹⁰ This is a primer for inequities, since individuals with LN who are from diverse racial/ethnic groups already experience disparities pertaining to their care, including delayed initiation of treatment.¹⁰ ICER makes a call to action for stakeholders—manufacturers, payers, researchers, and professional organizations—to ensure that the market entry of these new therapies leads to a reduction in health inequities in LN.

First, in addition to improving the representation of non-White patients in clinical trials, manufacturers should steer away from creative ways to extend patent protection that may come at the expense of patient affordability and access to timely and important care.¹⁰ This is of relevance because Aurinia Pharmaceuticals filed a patent for voclosporin's dosing protocol, which may delay generic entry until 2037. The preclusion of generics from entering the market has the potential to exacerbate disparities, since generics have lower out-of-pocket costs and are often more affordable for patient groups experiencing disadvantages. In fact, prescription drug costs are more likely to be a barrier to medication use for racial and ethnic minority populations compared with White populations.¹⁶

Payers have a major role in ensuring equity in access to belimumab and voclosporin. Managed care plans can help address disparities through the design of coverage policies that consider patients' racial/ethnic background and, particularly, differences in disease outcomes, treatment responses, and living conditions.¹⁷ In designing such policies, payers should consult with patient groups from diverse

backgrounds.¹⁶ Once coverage policies are implemented, payers should collect data and assess how such policies affect use of medications among different racial/ethnic groups. These quantitative assessments would determine whether coverage criteria perpetuate or mitigate disparities in medication use and subsequent health outcomes.

Second, another opportunity for payers to reduce health inequities is the development of quality measures and assessments that account for race/ethnicity and other sociodemographic factors such as geographic location, sex, and primary language.^{18,19} Quality measures that quantify receipt and adherence to belimumab and voclosporin among LN patients who are eligible to receive these therapies can optimize the use of these new medications. The stratification of such measures by race/ethnicity can ensure that quality measures are met by all beneficiaries and not only by a particular group of people, thus, reducing disparities. For example, Michigan Medicaid evaluated postpartum care as a quality measure among pregnant women.¹⁹ Overall results showed that 61% of pregnant women received recommended postpartum care. However, when race/ethnicity was factored in, results showed prominent disparities between Black and White women, with 63% of White women receiving postpartum care compared with 54% of Black women.¹⁹ The stratification of quality measures by race/ethnicity was actually proposed by the Centers for Medicare & Medicaid Services in its Quality Strategy to address health equity in Medicaid.^{19,20}

Finally, the ICER report urges researchers and professional societies to contribute to the generation of evidence and clinical guidelines that help reduce health inequities. Given the low representation of non-White patients in the clinical trials that evaluated belimumab and voclosporin, rigorous observational studies to assess real-world heterogeneities in treatment response are warranted. Specifically, observational researchers can contribute to improving health equity by conducting studies that evaluate long-term health outcomes of belimumab and voclosporin in diverse real-world populations.¹⁰ Furthermore, research focused on biomarkers that can predict response to treatment will be essential in guiding the appropriate use of medications in certain patients.¹⁰ In the same vein, ICER invites professional societies to develop timely guidelines that address racial and ethnic disparities in treatment to guide clinicians and payers.¹⁰

We commend ICER for its timely assessment of the cost-effectiveness of voclosporin and belimumab as add-on agents to standard combination therapy for the treatment of LN. We acclaim and join its call to action for all stakeholders to contribute to overcoming health inequities in

the implementation of these novel therapies in clinical practice.

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