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Perspective

Note on Belimumab in Treatment of Lupus Nephritis

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DESCRIPTION

Systemic Lupus Erythematous (SLE) is a chronic autoimmune disorder that causes multisystem inflammation and organ damage. Lupus nephritis, which affects 25 to 60% of SLE patients, is the most prevalent severe manifestation of SLE and a leading cause of disease and mortality. Despite intensive treatment, the percentage of patients who have a renal response remains very low, and 10 to 30% of patients with lupus nephritis progress to end-stage kidney disease. This danger has been constant over the last three decades. SLE patients continue to have several requirements, including impaired quality of life, emotional problems, decreased job productivity, the need for unplanned medical visits owing to uncontrolled disease activity, and increased mortality. All of these requirements are linked by a similar thread which includes the increased organ damage caused by SLE patient's prolonged disease activity and drug-related adverse effects, particularly those associated with chronic corticosteroid use. Furthermore, there is no shared treatment protocol in SLE for long-term management and is frequently dependent on a single physician's experience.

Belimumab is a monoclonal IgG antibody that targets soluble B Lymphocyte Stimulator (BLyS). It decreases accessible BLyS levels for auto reactive B cell selection and survival. Belimumab was permitted in recent years for the treatment of systemic lupus erythematosus (SLE), and it is notable that it was the solely approved medicine. In last 60 years, the release of hydroxychloroquine, corticosteroids, and nonsteroidal anti-inflammatory drugs for SLE became more common. As a result, until 2011, lupus treatment primarily relied of corticosteroid and antimalarial use in combination with traditional immunosuppressants, rituximab. As a result, care of such a varied disease did not benefit from optimal treatment regimens, which may explain why SLE patient's long-term prognosis has remained poor. Indeed, across diverse lupus cohorts, excellent disease management with continuous remission is still rare, and the risk of organ deterioration in SLE patients has hit a plateau in the last decades, indicating that a balance between therapy-related benefits and damage has been attained. Even though the overall impact in the successful phases 3 Randomized Controlled Trials (RCT) was not sucessful, the approval of belimumab aroused high expectations for SLE. However, researchers must now discover whether belimumab is capable of actually improving patient's prognoses, in addition to the demonstrable benefit acquired in those tests. Because the follow-up period has been limited since its approval, researchers may focus on the main predictors of damage in SLE and see if belimumab may suppress those predictions.

The Food and Drug Administration authorized belimumab as a result of two key phases, 3 clinical studies of intravenous belimumab in patients with SLE (Belimumab in Subjects with Systemic Lupus Erythematosus BLISS-52 and BLISS-76). However, the individuals with severe and acute lupus nephritis were excluded from those studies; there is a lack of evidence on the effectiveness and safety of belimumab in patients with active lupus nephritis. A post-hoc analysis of BLISS-52 and BLISS-76 individuals who had proteinuria found that patients who received belimumab have decreased incidence of renal flares and lower proteinuria. These findings prompted to launch of the Belimumab International Study in Lupus Nephritis (BLISS-LN) to assess the safety and effectiveness of belimumab in combination with conventional treatment in patients with active lupus nephritis.

Following the BLISS trials, several case series and case reports were conducted, all of which agreed on belimumab's ability to improve disease activity control and reduce daily corticosteroid intake, which is expected to reduce organ damage in the future. Unfortunately, due to retrospective observations affected by clinical practice, those investigations did not systematically quantify disease activity according to authorized ratings. In 2014, researchers prospectively monitored 188 patients on belimumab and found that the majority of them improved significantly on the SLE Responder Index-4 (SRI4). Following that, they published the first prospective study on belimumab use as an on-top treatment in SLE with a 24-month follow-up. It should be noted that, while 73.1 percent of patients including were undergoing immunosuppressive therapy while receiving belimumab, a significant percentage of patient's not treated.

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Thus, the question remains whether belimumab should be used only after immunosuppressants have failed or even before immunosuppressants are used. In this regard, it is worth noting that acute manifestations, such as skin or joint disease, benefit the most from belimumab treatment when compared to chronic manifestations; as such, it is reasonable to consider belimumab as a useful drug when dealing with active disease symptoms before they become chronic. Furthermore, for individuals, using an off-label medicine as a first c hoice is better than using the familiar, but never-approved-for-SLE, standard immunosuppressants.

CONCLUSION

In conclusion, the patient who has an active disease with acute mucocutaneous, musculoskeletal symptoms, active serology, and disproportionate corticosteroid consumption, with a relapsing-remitting history is suitable for the usage of belimumab. However, due to its beneficial effects in preserving corticosteroids and improving disease control activity, any patient without severe lupus nephritis, active neuropsychiatric SLE or life-threatening SLE-related symptoms are eligible for belimumab usage.