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BELIMUMAB FOR SYSTEMIC LUPUS ERYTHEMATOSUS: FROM MECHANISM OF ACTION TO PERSONALIZED THERAPY

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Systemic Lupus Erythematosus (SLE) is a chronic, heterogeneous autoimmune disease characterized by loss of immune tolerance, autoantibody production, and multi-organ inflammation. It predominantly affects women of reproductive age and involves complex interactions between genetic, environmental, hormonal, and immunological factors. Central to SLE pathogenesis is defective clearance of apoptotic and necrotic debris, leading to persistent exposure to autoantigens. This triggers activation of B and T lymphocytes, formation of immune complexes, and production of pro-inflammatory cytokines, particularly type I interferons.

Lupus nephritis (LN), a severe manifestation occurring in up to 40% of patients, results from immune complex deposition in renal structures. Clinical outcomes depend on the location of these deposits: subendothelial accumulation leads to proliferative forms (classes III/IV) with significant inflammation, while subepithelial deposits are associated with membranous LN (class V), characterized by heavy proteinuria. Tubulointerstitial inflammation further contributes to chronic kidney damage and fibrosis.

Belimumab, a fully human monoclonal antibody targeting B cell activating factor (BAFF), represents a major advancement in SLE therapy. By inhibiting BAFF, belimumab reduces B cell survival, differentiation, and autoantibody production. Its efficacy was demonstrated in pivotal clinical trials (BLISS-52 and BLISS-76), leading to its approval for active SLE in 2011 and later for LN following the BLISS-LN trial in 2020. These studies showed that belimumab, when added to standard therapy, improves disease control and reduces flare rates.

Standard SLE management includes hydroxychloroquine for all patients, glucocorticoids for disease control, and immunosuppressants such as mycophenolate mofetil, azathioprine, or methotrexate for steroid-sparing effects. Cyclophosphamide is only used for serious illnesses that endanger organs. In LN, induction therapy typically involves mycophenolate mofetil or cyclo-phosphamide, followed by maintenance therapy with mycophenolate or azathioprine. Treatment goals emphasize disease remission, prevention of organ damage, and in LN, progressive reduction in proteinuria and preservation of renal function.

Despite the strong evidence base and the inclusion of belimumab in international guidelines (American College of Rheumatology (ACR) 2025, European Alliance of Associations for Rheumatology (EULAR) 2023, Kidney Disease Improving Global Outcomes (KDIGO) 2023), the drug is currently not registered in the Republic of Belarus. For example, in Russia, since 2019, the drug has been approved for use in children aged 5 years and older with active systemic lupus erythematosus.

Current guidelines recommend belimumab as an add-on therapy in patients with persistent disease activity or frequent flares despite standard care. Emerging strategies include combination therapy with rituximab and biomarker-driven approaches to optimize patient selection. Potential biomarkers include circulating BAFF levels, interferon signatures, and specific autoantibody pro-files.

In conclusion, belimumab exemplifies mechanism-based therapy in autoimmune disease, offering a targeted approach to modulating B cell activity in SLE and LN. While its role continues to evolve, particularly in combination regimens and personalized medicine frameworks, further research is needed to refine its optimal use and integrate it with emerging biologic therapies.