Systemic autoimmune diseases are complex multisystemic illnesses whose management may involve any specialty, although the most closely involved physicians are normally rheumatologists and internists.

The majority of systemic autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, progressive systemic sclerosis, primary Sjögren syndrome, inflammatory myopathies, and ANCA-associated vasculitis, have been treated principally with cytotoxic agents and corticosteroids, which, although effective in improving disease manifestations and survival, produce severe adverse events and do not prevent relapses, while a varying proportion of patients are refractory to treatment. The need for safer, more effective drugs, together with increased knowledge of the pathogenesis of autoimmune diseases is reflected by the interest shown in biologicals, with clinical trials of the B-cell depleting agent rituximab arousing great hope.

Indeed, the emergence of B-cell-targeted therapies has opened a new era in the therapeutic approach to systemic autoimmune diseases. Four agents deserve specific mention: (1) rituximab, used since 2002 in nearly 2,000 reported patients (1,000 in uncontrolled studies). In 2011, the US Food and Drug Administration (FDA) approved rituximab plus glucocorticosteroids as a front-line therapy for adults with granulomatosis with polyangiitis (Wegener’s granulomatosis) and microscopic polyangiitis. This new indication for rituximab represents the first ever FDA-approved therapy for these two diseases and the first alternative to cyclophosphamide for the treatment of severe disease in nearly four decades. Rituximab has also been successfully deployed in other autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, mixed cryoglobulinemia, primary Sjögren syndrome, inflammatory ocular disorders, and hematological autoimmune disorders and has been shown to be suitable for patients refractory to conventional immunosuppressant agents; (2) belimumab, which has been tested in more than 2,000 patients in controlled trials, was approved by the FDA and the European Medicines Agency (EMEA) in 2011 for the treatment of systemic lupus erythematosus; (3) epratuzumab, tested in trials including nearly 300 patients; and (4) ocrelizumab, trials of which have recently been halted due to an unexpectedly high rate of severe infections.
The use of B-cell-depleting agents in clinical practice, overwhelmingly restricted to rituximab, is principally centered on patients who do not respond or are intolerant to standard therapy and those with life-threatening presentations. Forthcoming studies of B-cell-directed strategies, particularly investigations of off-label rituximab use and post-marketing studies of belimumab, will provide new insights into the utility of these treatments in the routine management of patients with autoimmune diseases. Careful evaluations of the risk/benefit profiles of these biologic agents will be essential as their full role in the treatment becomes established.

The main objective of *Drugs targeting B-cells in autoimmune diseases* is to offer the reader the latest opinions of the leading international clinical experts on the practical use of biological agents directed against B cells in autoimmune disorders, both systemic and organ specific. Clinical guidelines for the correct use of these agents can only be made by a restricted number of physicians with long clinical and research experience.

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