

OPINION ARTICLE

## Present and Future of Biologic Therapy in Dermatology

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The appearance in recent years of a new series of drugs known as “biologics” has led to major changes in the therapeutic management of various diseases. The first problem lies in defining those substances known as biologic drugs or biologic response modifiers, as the generic term covers a large group of substances obtained by means of genetic engineering, including hormones, neuroactive compounds, and immunoreactive compounds that act at a cellular level and that are used in the treatment, prevention, and cure of human diseases.

In traditional conventional drugs the mechanism of action is not strictly specific to a particular disease, while, in most cases, the creation and use of biologics builds on intrinsic knowledge of the pathologic mechanisms of the disease. These drugs are thus designed specifically to interfere with, block, or cancel an individual step in the immunopathological pathway of the disease.

In dermatology, we use biologic agents that fundamentally consist of proteins and that are primarily designed to bind extracellular targets. At present we basically use 3 types of molecules: recombinant human cytokines, monoclonal antibodies, and fusion proteins.

Over the past decade, the use of these drugs has revolutionized the treatment of various dermatological diseases, leading to improved prognosis, control of symptoms, and in some cases, prevention or avoidance of complications.

The disease most affected by this change in therapeutic options has been psoriasis, due to both the large number of patients involved and the social impact of the condition. Psoriasis is an, as yet, incurable, chronic illness with a course that involves outbreaks, and that affects approximately 2.5% of the general population. As a result of the skin and joint symptoms associated with the condition, it implies not only high drug costs, but also, even more importantly, a high social cost associated mainly with absenteeism. Also, at present many patients are not satisfied with the outcome of treatment with the drugs traditionally used to control

the condition. Similarly, the pathogenesis of psoriasis itself carries with it a higher rate of comorbidity; the condition known as metabolic syndrome (obesity, smoking, hypertriglyceridemia, increased cardiovascular risk, and hypertension) is more common amongst these patients. Psoriasis can have a large impact on the quality of life of a patient, meaning that the condition should be regarded not exclusively as a skin condition, but as a systemic problem to be tackled continually with systemic and multidisciplinary approaches.

The advent of biologics has resulted in changes in the treatment and progression of psoriasis; these drugs block costimulatory pathways by neutralizing cytokines or restoring the immune cell balance. The existence of a specific target cell has made these drugs far safer and more effective than traditional oral therapies, whose intrinsic toxicity made periodic usage—known as rotational or sequential treatment—necessary and prevented sustained improvements from being obtained over extended periods of time.

One of the most important advantages of biologics is their effectiveness. The fact that they interfere with a step in the pathogenic mechanism of the disease means they offer therapeutic exclusiveness, which translates into increased clinical efficacy. However, in some cases the response is varied or incomplete, indicating that there are genotypic subgroups in psoriasis that produce different immune responses.

Safety is a main cause for concern in the use of these drugs, but it must be borne in mind that they are backed by a large number of clinical trials and that, in many cases, their use in treating similar diseases—such as rheumatoid arthritis—provides us with better knowledge of their long-term safety profile. An associated increase in the incidence of bacterial infections has already been identified, above all in the respiratory tract, but these are generally mild and do not imply an increased risk. However, an increased incidence of tuberculosis has also been described for some of these drugs. It is therefore essential that patient selection and monitoring criteria be strictly applied, in order to avoid risks of all types—infection, tumors, or cardiovascular risks. We must not forget that these substances alter the immune response and can possibly, in the long term, lead to tumors or other complications. Nonetheless, a distinction would have to be drawn between those complications directly attributable to these drugs and those attributable to the

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disease itself or to previous treatments. Therefore, clear clinical guidelines must be established in order to set standards for correct usage and to support dermatologists in rationalizing use. These guidelines must be adapted to the characteristics of Spain, just like those already in place in other countries.

Despite the fact that we are fundamentally working with only 3 families of biologic agents, many therapeutic possibilities exist and these are only the first generation drugs. In the future, new, far more selective drugs will undoubtedly appear—some are already in the research or development stages—and these will offer greater effectiveness with fewer side effects. Current studies are looking into adding new molecules to the list of biologics already on the market and available for use—for example, interleukin (IL)-12, and IL-23—and that offer an even more comfortable dosage than presently available drugs.

Many other skin conditions have also benefited from the use of biologics: lymphoma, pemphigus vulgaris, systemic lupus erythematosus, dermatomyositis, atopic dermatitis, sarcoidosis, granuloma annulare, hidradenitis suppurativa, pyoderma gangrenosum, bullous pemphigoid, Behçet disease, pityriasis rubra pilaris, etc. However, accumulated experience in the use of biologics is far more limited for these conditions, and when biological therapy is selected it is important to be aware of the mechanism of action of the drug in the context of the pathophysiology of the disease.

In summary, the results obtained so far in this new field have been very encouraging, and they offer the promise of an expanding range of treatments for a great many skin conditions in the future, once the long term adverse effects—above all, the incidence of severe infection, and predisposition to lymphoma, internal tumor, and skin cancer—are minimized or made to compare favorably to the rates for other commonly used drugs.

#### **Conflicts of Interest**

The authors declare no conflicts of interest.

### **Recommended Reading**

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