Editorial

A new era in psoriasis and psoriatic arthritis therapy: new mechanisms of action and the introduction of biogeneric drugs

Uma nova era na terapia em psóríase e artrite psoriática: novos mecanismos de ação e a introdução de biossemilares

Interleukin-17 is a proinflammatory cytokine that acts by increasing the expression of chemokines that recruit monocytes and neutrophils to the site of inflammation. Produced by helper T cell subtypes and induced by other interleukin (IL23), IL17 initiates its function by joining itself to a cell membrane receptor (IL17R). The neutralization of this function by the blockage of this union to the receptor, or by the administration of a specific antibody against interleukin, entails the possibility of a new biological treatment of autoimmune diseases such as Psoriasis and Psoriatic Arthritis.2,3

The introduction of a new biological, with a new mechanism of action, means that the history of biological therapies for psoriasis and other autoimmune diseases will be re-written. The neutralizing monoclonal antibody, IL17 (secukinumab), should be approved by ANVISA by the end of 2005 or beginning of 2006.2 US Food and Drug Administration (FDA) recommended an almost unanimous approbation of secukinumab for the treatment of psoriasis; and this drug was approved months ago by the European Medicines Agency (EMA) under the trade name Cosentyx. Two other biological agents should become widely available soon: Ixekizumab and brodalumab, a anti-IL-17 receptor monoclonal antibody. What draws more attention in the studies which led to the approval of anti-IL17 is that those papers that carried out head-to-head comparisons between etanercept and ustekinumab – which are part of the standard therapy with biological agents for psoriasis – show that anti-IL17 features have superior clinical efficacy versus anti-TNF and anti-IL12-23.

In a study including 1307 patients receiving secukinumab, the response to anti-IL17 was more robust when compared to etanercept. When compared to ustekinumab after 4 months in a phase III study, most of patients achieved PASI 90 in a more significant percentage, when compared to the group treated only with ustekinumab. Similarly to what seems to occur in patients with rheumatoid arthritis, small molecules should also play a role in the treatment of psoriasis and psoriatic arthritis. This is indeed the case of Apremilast, an inhibitor of phosphodiesterase and modulator of cAMP levels, which has recently been approved by FDA. One aspect that brought some controversy regarding the analysis of the clinical studies was that, in the approval of this agent, body mass was not considered (patients with psoriasis tend to be obese when compared to individuals of the same age but without psoriasis). The other aspect to consider is that, even not being a biological agent, but a synthetic one, pharmaceutical companies are introducing the drug on the market with prices similar to those practiced for biological agents.5-10 IL17 is a proinflammatory cytokine that plays an important role in perpetuating the psoriatic plaque. The receptor for IL17 can be found on the surface of keratinocytes, and its blockage reverses the histopathology of the psoriatic lesion. With anti-IL17, it is possible to obtain an almost complete whitening of skin lesions, besides a simultaneous improvement of the associated arthritis, especially if this is the first biological used. Similarly to what occurs in rheumatoid arthritis and psoriasis, after 3 years of treatment, less than half of the patients who had been initially benefited with favorable responses still present convincing clinical responses. This phenomenon, also known as “biological fatigue”, seems to be common in rheumatic patients and with plaque psoriasis.

Adverse effects of anti-IL17 are more infectious in nature, but do not appear to be an important problem when compared to those stemmed from the use of anti-TNFs. As a little less than half of patients with psoriasis have joint manifestations, Phase III studies evaluating anti-IL17 are underway, some of them in their final phase of evaluation. The strategy of cytokine IL17 blockade in inflammatory arthritis and, in particular, in psoriasis, should pave the way for a new phase in the arsenal of biological agents, especially considering that the market should make available anti-TNF biogeneric drugs soon.
Conflicts of interest

The author declares no conflicts of interest.

REFERENCES


Morton Scheinberg\textsuperscript{a,b}

\textsuperscript{a} Hospital Israelita Albert Einstein, São Paulo, SP, Brazil
\textsuperscript{b} Center for Clinical Research, Hospital AACD, São Paulo, SP, Brazil

E-mail: morton@osite.com.br

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