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Review Article

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Biotherapies in Psoriasis Treatment

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ABSTRACT

Biotherapies occupy an increasingly important role in the arsenal of systemic treatment of moderate to severe psoriasis. The most used molecules in practice are anti-TNF alpha and interleukin inhibitors. International recommendations were established by European and English experts specifying the place of these treatments in the therapeutic strategy of the psoriasis.

Keywords: Psoriasis; Biotherapies; Anti TNF alpha; Interleukin inhibitors; Recommendations

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INTRODUCTION

Psoriasis is a chronic inflammatory dermatosis, affecting 2-3% of the population [1]. It is due to immune system disorder. The advent of biotherapies, aiming to block or inhibit the key effector mechanisms in the pathophysiology enhanced its therapeutic arsenal and significantly changed patients' management with moderate to severe psoriasis [2], with an estimated improvement 70% in medium term [3].

Biotherapies most use in practice in psoriasis

Conventional systemic treatments are known for their organ specific toxicity cumulative dose dependent and inconsistent efficiency limiting their continuous use [1]. The research on psoriasis's pathophysiology, helped to highlight the key role of immune cells and cytokines such as Tumor Necrosis Factor (TNF) in its occurrence [1]. Thus new drugs called "biotherapies" were created and were a main advance in the treatment of moderate to severe psoriasis [4].

Infliximab

It is a chimeric monoclonal antibody (IgG1) bivalent fixing TNF alpha, in its soluble and membrane form, thus inhibiting its biological activity. Originally used in rheumatoid arthritis and in Crohn's disease. In 2005, it received the marketing authorization in plaque psoriasis. Its prescription is based on an induction phase followed by a maintenance phase at the fourteenth week, in case of therapeutic response. Several randomized controlled clinical trials evaluating Infliximab efficiency in psoriasis were published, showing that the rate of patients achieving PASI75 was 75 to 88% at 3 months, 75-82% at 6 months and 52 to 61% at 12 months. However, this efficiency is sometimes impaired by the presence of antibodies to Infliximab which reduce its therapeutic efficiency and tolerance [1-5].

Etanercept

It is a human protein of recombinant fusion, consisting of the shortened extracellular portion of membrane TNFR2 / p75 and of the hinge region of the Fc fragment (CH2 / CH3) of an IgG1. This soluble receptor fixes TNF alpha soluble and transmembrane, and competitively inhibits the binding of TNF alpha to its cell receptors. Initially

prescribed for rheumatoid arthritis, has obtained marketing authorization for psoriasis in 2004. Many randomized controlled clinical trials evaluating the efficiency of Etanercept in psoriasis have also been published, showing that patients proportion achieving the PASI75 was Etanercept respectively 25 and 50 mg 2x/week from 29 to 34% and from 48 to 54% at 3 months, 46 to 60% and 60% at 6 months and 55% and 63 % at 12 months. During the first 6 months of treatment, anti-Etanercept antibodies were detected at 0 to 2.7% of patients, these antibodies were neutralizing in vitro, and their presence was not related to efficiency or tolerance [1-6-7].

Adalimumab

It is a monoclonal bivalent human antibody IgG1, anti-TNF alpha, it blocks the interaction between TNF alpha and p55 label and p75 cellular receptor. Initially prescribed for rheumatoid arthritis in 2007, it obtained the marketing authorization for moderate to severe plaque psoriasis. Of all the available randomized controlled trials assessing Adalimumab at a dose of 40 mg / 2 weeks, the proportion of patients achieving the PASI75 was 49 to 77% at 3 months, 59 to 70% at 6 months and 56% at 12 months. However, few data are available on the appearance of anti-Adalimumab antibodies during treatment with this molecule. Tolerance was not correlated with these antibodies presence [1-8].

Ustekinumab

It is a human monoclonal antibody specific to the p40 subunit common to interleukins 12 and 23. Its efficiency and tolerance have been shown Compared to placebo in randomized Phase III trials, double-blind, showing that patients proportions reaching the PASI75 at week 12 were 67%, 66 to 76% and 3-4%, respectively, after subcutaneous injection in 0 and day 28 of Ustekinumab 45 mg Ustekinumab 90 mg and placebo. The safety profile was comparable to 12 weeks under Ustekinumab and placebo [1-9].

Secukinumab: A new Molecule under test

Secukinumab is a fully human anti IL-17A monoclonal antibod. A pooled analysis of 10 phase II and III clinical studies in patients with moderate to severe plaque psoriasis (analysis included 3993 subjects, 3430 received secukinumab. Over 52 weeks, for secukinumab 300 mg, 150 mg, and Etanercept, respectively), supports the favorable safety profile of secukinumab. A similar safety profile was observed in the 300 mg and 150 mg treatment groups and in terms of safety, was comparable to Etanercept over 52 weeks in patients with moderate to severe plaque psoriasis. Extension studies are ongoing to further confirm the longer-termsafety experience with secukinumab in psoriasis [10].

Recommendations for biotherapies use in moderate to severe psoriasis

Biotherapies have an increasingly important role in the arsenal of moderate to severe psoriasis. In practice, the most used molecules are three anti-TNF alpha (Infliximab, Etanercept and Adalimumab) and an inhibitor of the p40 subunit of interleukins IL-12 and IL-23 (Ustekinumab). International experts (European and British) have established recommendations stating the importance of biotherapy in the treatment strategy of moderate to severe psoriasis [11]:

-The biotherapies are reserved for the chronic and severe forms of plaque psoriasis, in case of failure, or contraindication or intolerance to at least two systemic therapies including ciclosporin, methotrexate and phototherapy.

- In European recommendations, eligibility criteria are moderate to severe psoriasis with a PASI> 10 and failed phototherapy (no response, contraindication or intolerance) and conventional systemic therapies.

-British recommendations go to the same sense. Eligibility criteria are severe psoriasis with a PASI≥10 (or affected body surface ≥10% if PASI not applicable) and DLQI I> 10, and at least one of the following criteria:

- Contraindication or an impossibility to use phototherapy or other conventional systemic treatments (toxicity or risk of clinically significant toxicity)
- Intolerance or lack of response to conventional systemic treatment
- Incompatible comorbidities taking systemic therapies (methotrexate, cyclosporine)
- Severe disease, unstable, life threatening

CONCLUSION

Biotherapies have been a therapeutic advance in the treatment of moderate to severe psoriasis. However, these treatments use must comply with international recommendations and should be subject to specific monitoring for their effectiveness and tolerance for longer use.

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