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Short Communication

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Janus Kinase Inhibitors: Hope for Biotherapy in Sub-Saharan Africa?

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Abstract

Introduction*: Tofacitinib is an oral Janus Kinase (JAK) inhibitor used in the treatment of rheumatoid arthritis (RA) and in many other conditions [1-3]. After promising results in clinical and preclinical trials, Tofacitinib was extensively evaluated in pivotal trials in 2012 and its efficacy on demonstrated structural damage [4]. Thus, Tofacitinib has been approved for the treatment of patients with RA who have an inadequate response to methotrexate [5].*

Biologics are used routinely in many countries but remain difficult to access in sub-Saharan Africa [6]. The cost of biotherapies, their side effects, in particular infectious ones, and their presentation in injectable form constitute a brake on the use of these new treatments. The advent of a new therapy administered by bone would represent an excellent alternative for Africa.

We thus report the case of a patient who failed conventional treatments and who has benefited from Tofacitinib (Xeljanz 5mg®).

Keywords: Janus kinase inhibitor, Rheumatoid arthritis, Africa

Clinical Case

Mr AY, 38 years old, has been followed for sequelae RA since 2015 under conventional treatment, csDMARDs (conventional synthetic Disease-modifying antirheumatic drugs) at optimal dose but with persistence of pain, biological inflammation and a DAS28 varying between 3 and 5 requiring corticosteroid dependence. The use of biotherapies is thus envisaged. As anti-TNFα was not available, treatment with Tofacitinib (Xeljanz®5mg) 10mg / day in two doses has been started in September 2018 in combination with MTX 10mg / week after a pre-treatment assessment, in particular infectious return to normal. There was dyslipidemia with a total cholesterol level of 2.40g / l and 1.71g / l for LDL-cholesterol. A first check was carried out after 1 month of treatment with good progress (DAS28 <2) and good tolerance of Tofacitinib. However, we noted a hypercholesterolemia at 2.49g / l and LDL-cholesterol at 1.71g / l motivating the setting on Atorvastatin 10mg / d and hygiene-dietetic measures with secondary normalization. Treatment has been interrupted in October 2019 following the unavailability of Xeljanz, but with continuity of Methotrexate 10mg / week. However, with a follow-up of six months, remission was maintained.

Discussion

The possibility of using small molecules capable of blocking key cytokines by targeting their signal transduction pathways with small molecules was recognized as early as 1995, but with many challenges [4]. In the case of our patient, Tofacitinib was chosen preferentially over anti-TNFs because of its greater accessibility (oral presentation vs. injectable for anti-TNFα), its cost, its best tolerance and in accordance with the recommendations of the EULAR [7, 5]. In addition, Tofacitinib has been shown to be non-inferior to MTX and Adalimumab and it is about as effective as Etanercept and Tocilizumab [1,4, 5, 7-9]. The only adverse effect noted in our patient was an increase in hypercholesterolemia but without an increase in cardiovascular risk. These results suggest that Tofacitinib may be a relevant option for patients where treatment with csDMARD is inappropriate or ineffective. But also, the most appropriate choice in situations where a biological agent is also inappropriate or not available, particularly in sub-Saharan Africa [9]. However, further studies are needed to assess the tolerance of Tofacitinib, its efficacy and its place in the therapeutic arsenal of chronic inflammatory rheumatism, in our context.

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