

Short communication

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## A New Era in Psoriasis and Psoriatic Arthritis Therapy: Drugs with New Mechanism of Action and the Option for the use Biosimilars

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### Short communication

Our ability to successfully treat patients with moderate to severe psoriasis has suffered a dramatic improvement over the past decade with the development of targeted therapies. The same applied to psoriatic arthritis where psoriasis can present associated with arthritis (synovitis) enthesitis, spondylitis, and extraarticular manifestations [1]. Treatment of Psoriasis and Psoriatic Arthritis changed dramatically since the introduction of anti TNF therapy drugs that were shown to improve signs and symptoms slow the progression of the inflammatory disease and the radiographic progression [2]. Not predicted in clinical trials but appearing on real life practice a variable percentage of patients show no clinical response and in some the initial positive response disappear in a variable period [3]. In addition it was also possible to find that in some patients anti TNFs can lead to a paradoxical effect where amelioration of the disease is replaced by

aggravation of the skin lesions [4-5] Fortunately, new pathogenetic mechanisms were discovered that can move the targeted therapy from blocking anti TNF to inhibit other pro inflammatory cytokines such as IL-12, IL23 and IL-17 and help patients where anti TNF therapy are no longer helpful for the reasons described above [5-6].

As previously suggested in a recent article the introduction of a new biologic with mechanism of action out of the TNF pathway and with initial results showing greater superiority when compared with other target therapies may lead to a first line option of therapy in Psoriasis and Psoriatic Arthritis [7]. IL-17 is a proinflammatory cytokine that plays a major role on the chronic perpetuation of the psoriatic plaque. The receptor for IL 17 can be found on the keratinocyte surface and blocking of its activity leads to a reversal of the histologic features of the plaque (Figure 1) [8].

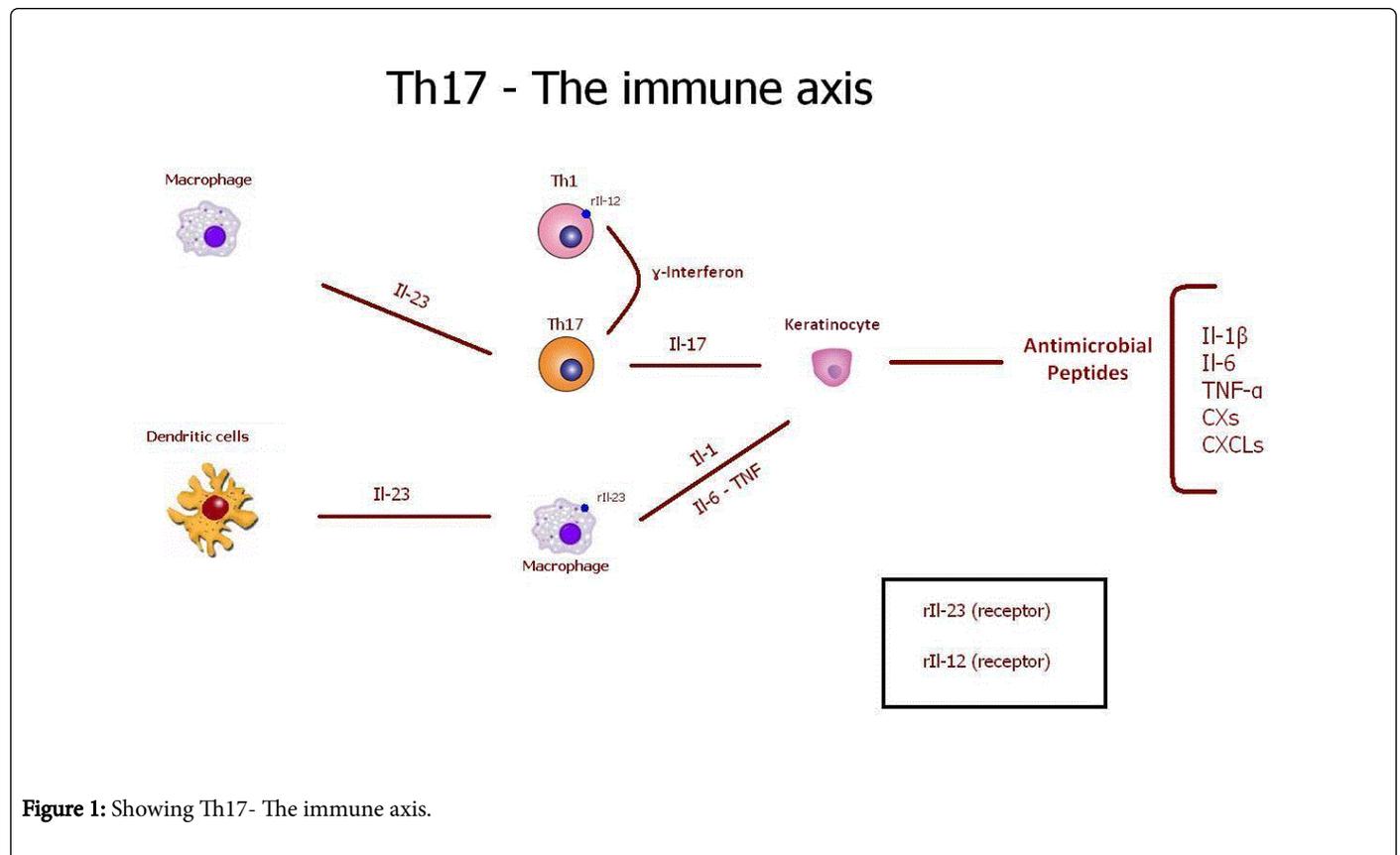
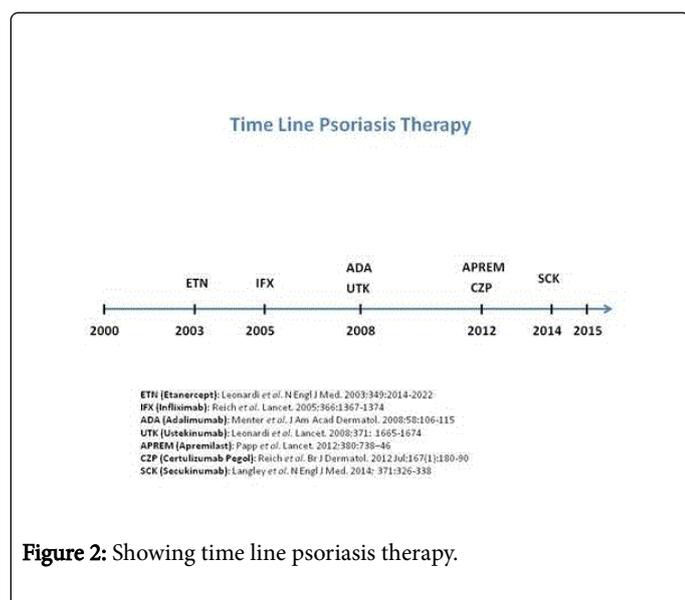


Figure 1: Showing Th17- The immune axis.

Apparently this is the case with secukinumab a monoclonal antibody against IL-17 that was approved by the European agency (EMA) and the FDA mid last year for the treatment of psoriasis [9-10]. Ixekizumab and brodalumab are also anti IL 17 medications that are still under clinical development for psoriasis [11]. When one look at the clinical trials one can find head to head comparison between anti IL-17 with etanercept and ustekinumab [12,13]. On the latter it was possible to demonstrate in a phase 3 clinical trial that a larger number of patients reached PASI 90 when compared with ustekinumab. In another study including 1307 patients secukinumab was compared with etanercept and the results point to a superior efficacy of anti-IL 17 when compared with the anti TNF. Anti-IL 17 continuous use leads to the clearing of the lesions and if arthritis is associated patients also show improvement of the joint disease. However, to what is known in rheumatoid arthritis after a three year period half of the patients may lose clinical response in a phenomenon now known as biologic fatigue. The adverse effects of continuous blocking of anti-IL 17 are of an infectious nature but substantially less than what we know about chronic use of anti TNF. Since approximately half of the patients with Psoriasis can develop or present with arthritis studies are underway in Psoriatic Arthritis some finished and some on its final part of the development [14].

Similar to what is happening in Rheumatoid Arthritis small molecules are being evaluated for the treatment of psoriasis and psoriatic arthritis. Apremilast a phosphodiesterase 4 inhibitor was recently approved for the treatment of both psoriasis and psoriatic arthritis, oral use twice a day. It is not well defined where Apremilast would fit into the various options of treatment now available. One of the problems with apremilast is that patients with psoriasis tend to be overweight the recommended dose does not take in consideration the weight of the patient [15]. Tofacitinib is under evaluation for psoriasis. Initial attempts to include the small molecule in the psoriasis are still pending by the FDA that suggested additional studies should be performed [16] (Figure 2).



Finally, the development of biosimilars although not a new mechanism of action are looking to be an alternative for psoriasis and

psoriatic arthritis patients that will be started with a TNF inhibitor and some studies are underway with all three TNF inhibitors etanercept, infliximab and adalimumab [17]. In fact, the FDA Arthritis Advisory Committee has recommended the approval of a biosimilar version of the TNF inhibitor infliximab for psoriasis and other immune inflammatory disorders as of February 2016 [18]. So the next decade will be plenty of new options for the treatment of Psoriasis and Psoriatic Arthritis, as the title suggests a new era for new mechanisms of action and other options.

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