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Clinical Effectiveness and Safety of Treatment With Anti–Tumor Necrosis Factor α Drugs in a Cohort of Colombian Patients With Rheumatoid Arthritis

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Objective: To compare the clinical response at 24 months and evaluate the adverse events (AEs) of patients with rheumatoid arthritis (RA) treated with etanercept 50 (injectable solution 50 mg prefilled syringe), etanercept 25 (lyophilized 25 mg), infliximab, adalimumab, or golimumab.

Methods: A cohort study was carried out in patients with RA, in treatment with etanercept (injectable solution 50 mg prefilled syringe or lyophilized 25 mg), infliximab, adalimumab, or golimumab. Duration of study: follow-up was carried out for 24 months. The difference of initial and final 28-joint Disease Activity Score, remission incidence, difference of initial and final Health Assessment Questionnaire score, disability recovery, and AE rate were evaluated.

Results: The study enrolled 435 patients (108 adalimumab, 107 infliximab, 92 etanercept 25 mg, 81 etanercept 50 mg, and 47 golimumab). For etanercept 50, the median difference between basal and at the end of follow-up 28-joint Disease Activity Score was 1.7. For golimumab, it was 1.4; for adalimumab, it was 1.1; for etanercept 25, it was 1.02; and for infliximab, it was 0.96 ($p = 0.001$). The median difference between basal and final Health Assessment Questionnaire ranged was 1.66 for etanercept 50, 1.34 for etanercept 25, 1.3 for golimumab, 1.24 for adalimumab, and 1.07 for infliximab ($p = 0.0005$). Comparatively, etanercept 50 presented the highest cumulative incidence (77%; 95% confidence interval [CI], 67%–86%) and remission incidence (64 cases per 100 person-months; 95% CI, 4.9–8.1 cases per 100 person-months) and the lowest AE rate (8.6 per 100 person-years; 95% CI, 5.3–15 per 100 person-years).

Conclusions: In patients with RA treated with anti–tumor necrosis factor α drugs, the highest incidence of remission and the lowest rate of AEs were documented for the cohort exposed to etanercept 50 mg.

Key Words: adalimumab, arthritis, etanercept, golimumab, infliximab, recovery of function, remission induction, rheumatoid

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Tumor necrosis factor α (TNF-α), interferons β and γ, and interleukins 1, 2, and 6 are part of the set of promoters of the inflammatory process, linked to the physiopathogenesis of rheumatoid arthritis (RA).[1,2] In the early stages of the disease, TNF-α is significantly expressed in the synovial tissue and locally stimulates the generation of neovascularization processes, promoting inflammation and increasing the production of other cytokines, which in turn favor the migration of white cells within the joint.[2,3] Based on this knowledge, the treatment of RA has been evolving during the last decades, and part of the available alternatives is focused on controlling this autoimmune phenomenon that causes an excessive inflammatory process.[4] Within these options, there are antirheumatic drugs of biological origin modifying the disease (disease-modifying antirheumatic drugs [DMARDs] biologic); some of them look for a specific effect on TNF-α and are known as anti–TNF-α drugs. In this group are etanercept adalimumab, golimumab, and infliximab, among others. All of them have proved to be effective and relatively safe, which has allowed them to be successfully included in the current RA treatment regimens.[5,6]

A key factor that has been described as a determinant of effectiveness is the adherence to medication, which in turn may be influenced by its route of administration and its dose frequency. It is for this reason that some authors have described that anti–TNF-α subcutaneous application can achieve better adherence rates than other orally administered drugs or other more complex schemes, which could translate into higher rates of clinical response.[7,8]

It is important to note that most of the evidence supporting the efficacy of anti–TNF-α comes from clinical trials in which, generally, the molecule of interest has been compared against placebo.[9] Despite the methodological advantages of these designs, because of their ability to control potential confounding biases, it is also important to bear in mind that these studies, by being ideally developed,[3,10–12] do not necessarily allow for finding out the effectiveness and performance of these drugs in conditions similar to those of real life and in direct comparisons with the best available treatments. Consequently, it is essential to have real-life data, in which it is possible to verify or contrast the clinical effect of these therapies, based on head-to-head comparisons.[13] Based on the above, the present cohort study was carried out, with the objective of comparing the 24-month clinical response and evaluating the adverse events (AEs) of a cohort of patients with RA treated with one of the following medications: etanercept 25 (lyophilized 25 mg), etanercept 50 (injectable solution 50 mg prefilled syringe), infliximab, adalimumab, and golimumab.

MATERIALS AND METHODS

Design, Population, and Sample

An observational cohort analytical study was conducted in a reference center for patients with RA who are treated under the concept of Center of Excellence in the city of Bogotá, Colombia. This institution has a registry of the patients treated, which made it possible to include the entire census of subjects older than 18 years, with a confirmed diagnosis of RA according to the criteria of the American College of Rheumatology/European League Against Rheumatism,[14] with active disease despite being in treatment with conventional DMARDs, for whom the attending physician considered starting a treatment scheme with one of the following biologic

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