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Predictive role of old and new diagnostic biomarkers regarding response to Etanercept therapy in rheumatoid arthritis

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Background: Introduction of biologic therapy has revolutionized the treatment of Rheumatoid Arthritis (RA) and many agents appeared in the last few years. Despite these advances, 20-40% of the patients are declared non-responder to at least one of the therapies.

Objective: Evaluating the predictive role for the response to etanercept therapy of Rheumatoid Factor (RF) isotypes IgM, IgA, anti-Cyclic Citrullinated Peptide (anti-CCP), anti-mutated citrullinated vimentin (anti-MCV), 14-3-3 ETA protein and Cartilage Oligomeric Matrix Protein (COMP). We have also assessed the status pretreatment of these biomarkers and the response to treatment. The last objective was to follow the evolution of serum levels of these biomarkers under biologic treatment.

Method: Prospective and observational study including 16 patients followed 12 months with active RA, uncontrolled by conventional synthetic DMARDs. Clinical assessment was performed at 0, 6 and 12 months according to ACR criteria approved by OMERACT and evaluation of treatment response according to EULAR criteria (good/moderate/non-responder).

Result: 13 patients (81.3%) were women and 3 (18.7%) men; the average age of the entire group was 58.5±8.5 years. At 6 months, 3 patients were declared non-responders, 9 achieved moderate response and 4 good response. Following baseline immunological parameters titers and the response at 6 months, general tests have identified significant differences between groups only for one of the six biomarkers studied. Lower baseline titers of 14-3-3 eta protein (0.25±0.38 mg/ml, p=0.01) had predictive value for achieving a good response at 6 months. After 12 months, 3 patients achieved moderate response and 10 good responses. At this evaluation, we didn't find significant differences between baseline immunological parameters titers and the EULAR response (moderate/good response RF type IgM=218.67±71.28/ 133.21±138.97U/ml, p=0.34; RF type IgA=142.57±139.55/13.70±14.29 U/ml, p=0.09; anti-CCP=91.80±50.33/75.09±51.75 mg/ml, p=0.63; anti-MCV=164.68±263.57/166.84±231.32 mg/ml, p=0.98; 14-3-3 eta protein 0.00±0.00/0.32±0.40 mg/ml, p=0.14; COMP=1055.9±130.50/895.1±209.98 mg/ml, p=0.24). Grouping patients in 2 categories (responders/non-responders), 14-3-3 eta protein maintained predictive value for the response at 6 months (p=0.01). Following the status pretreatment of biomarkers and EULAR response to etanercept therapy, we identified differences almost significant for 14-3-3 eta protein at 6 months, all 3 patients declared non-responders were 14-3-3 eta positive, and only 3/9 (33.3%) from those with moderate response and 1/4 (25%) of good responders were tested positive (p=0.0504). Regarding the evolution of serum levels, we noticed a reduction for all biomarkers tested, statistically significant only for COMP, baseline (938.34±189.68 ng/ml) versus 12 months (719.32±184.97 ng/ml, p=0.02).

Conclusion: 14-3-3 eta protein could be one of the biomarkers for identifying pretreatment the patients who will respond to biologic therapy in rheumatoid arthritis.

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