AB0303

PREDICTORS OF SERIOUS INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TARGETED THERAPY.

E. Koltsaeva1,2, G. Lukina1,2, E. Shmidt1, K. Lytikina1, E. Zhilyaev1,2,3. 1Research Institute of the Organization of Health and Healthcare Management, Moscow, Russian Federation; 2AS Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation; 3N.N. Bubnov Research Institute of Rheumatology, Moscow, Russian Federation; 4NI Firogov City Clinical Hospital 1, Moscow, Russian Federation; 5City Clinical Hospital, Moscow, Russian Federation; 6European Medical Center, Moscow, Russian Federation; 7Russian Medical Academy of Continuous Professional Education of the Ministry of Healthcare of the Russian Federation, Moscow, Russian Federation

Background: The problem of infectious complications in patients receiving bDMARDs deserves special attention. Serious infectious adverse events (SIAE) are a most important issue. To develop measures for their prevention it is necessary to know the predisposing factors.

Objectives: to detect predictors of serious infections among patients with rheumatoid arthritis receiving targeted therapy.

Methods: The study includes patients with rheumatoid arthritis from the Moscow Unified Arthritis Registry (MUAR), receiving treatment with biologics or tofacitinib. Search for predictors was carried out in two steps. At first step we selected patient related predictors (confounders) that significantly correlate with risk of SIAE. At the second step in the Cox risk regression model by forward stepwise selection, independent significant predictors of risk, which demonstrated significant correlation with development of serious infections, were found. Data about the treatment was added to the generated model: used targeted DMARDs, doses of glucocorticoids (GC), doses of methotrexate (MTX).

Results: Analysis includes 1052 treatment events in 772 patients. There were 44 serious infections. The mean age was 57.1 ± 12.8 years. The mean observation time was ~5.3 years. Independent patient related predictors of SIAE risk were the age RR - 1.12 per year (CI: 1.06-1.19), the age of onset disease RR - 0.94 per year (CI: 0.90-0.98), the year of inclusion in the registry RR - 0.64 per year (CI: 0.49-0.85). The dose of MTX and the doses of GC positively correlate with SIAE risk. RR for MTX is 1.05 per mg (CI: 1.005-1.109), RR for GC - 1.11 per mg (CI: 1.004-1.236).

Conclusion: Higher doses of methotrexate and glucocorticoids are independent significant predictors of serious infections in RA patients receiving targeted DMARDs.

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AB0304

IMMUNOGENICITY OF BIOLOGIC DRUGS IN THE CLINICAL PRACTICE IN THE BULGARIAN POPULATION OF PATIENTS SUFFERING FROM RHEUMATOID ARTHRITIS

K. Kraeva1,2, M. Geneva-Popova1,2, S. Popova1,2. 1Medical University - Plovdiv, Department of Protoendexics of Internal Diseases, Plovdiv, Bulgaria; 2University Hospital Kaspiela, Clinic of Rheumatology, Plovdiv, Bulgaria; 3University Hospital “St George”, Clinic of Rheumatology, Plovdiv, Bulgaria

Background: Biological drugs are protein derivatives that, as such, are highly immunogenic. In recent years there have been many conflicting opinions about the role of drug immunogenicity in clinical practice.

Objectives: To evaluate the drug immunogenicity of TNF-alpha blocking drugs (etanercept and adalimumab) used to treat patients with rheumatoid arthritis. To determine whether their presence can alter the effect of treatment and to evaluate their role in the clinical practice of rheumatologists.

Methods: 121 patients with rheumatoid arthritis, as well as 31 healthy controls, similar in sex and age, were examined. They were all monitored at 0, 6, 12 and 24 months from the start of TNF-alpha blocker treatment. Demographics, vital signs, markers of inflammation such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and disease activity indices were examined at each visit, respectively. Drug-induced neutralizing antibodies, as well as drug bioavailability in patients treated with adalimumab, were examined by ELISA.

Results: Drug-induced neutralizing antibodies to adalimumab were detected in 11.57% of patients at 6 month, in 17.64% of patients at 12 month, and 24.8% at 24 month. Drug-induced neutralizing antibodies to etanercept were not detected at 6 months, at 7.77% at 12 months, at 9.63% of patients at 24 months. Of the adalimumab patients who were having drug-induced antibodies, 92.59% had low drug bioavailability, while the remaining 7.41% of patients showed normal drug bioavailability despite the presence of drug-induced neutralizing antibodies. In terms of worsening of the disease activity, a positive correlation was found with the presence of drug antibodies - Pearson Correlation = 0.701, p = 0.001. Patients with poor clinical response and available drug antibodies receiving adalimumab were slightly more than those treated with etanercept at 12 and 24 months but the difference is non-significant-U = 0.527, p > 0.05 and U = 0.623, p > 0.05, respectively.

Conclusion: Presence of drug-induced neutralizing antibodies in patients treated with adalimumab and etanercept has been associated with poor clinical response and worsening of the patient’s condition. Testing of drug-induced neutralizing antibodies as well as the drug bioavailability of the drug used can be used as reliable biomarkers in clinical rheumatology.

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AB0305

STUDY OF CORRELATION OF B-CELL LEVEL AND PROGRESSION OF BONE DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING RITUXIMAB THERAPY

A. Kudryavtseva1, G. Lukina1, A. Smirnov2, S. Glukhova3, E. Aronova4, G. Gridneva5. 1V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; 2GBUZ Moscow Clinical Scientific Center named after Loginov MHD, Moscow, Russian Federation

Background: Rheumatoid arthritis is a chronic autoimmune disease characterised by inflammation of the synovial tissue and destruction of the underlying cartilage and bone. The goal of antirheumatic treatment is not only to attenuate the clinical symptoms of joint inflammation, but also to inhibit the progression of joint destruction. Rituximab - it is a chimeric monoclonal antibody that targets the CD20 molecule expressed on the surface of B cells. It has been successfully used to treat rheumatoid arthritis, and it is worth noting that its antidestructive effect sometimes does not meet the clinical.

Objectives: The aim of our study was to evaluate the correlation between the degree of B-cell depletion and the development of the clinical and antidestructive effects of Rituximab (RTM) therapy in patients with rheumatoid arthritis (RA).

Methods: The study included 108 patients (pts) with rheumatoid arthritis, most are middle-aged women with high disease activity (mean DAS28 6.1±1.04, RF-positive 77%, ACCP-positive 83%) treated with RTX (1000 mgx2 or 500 mgx2). Clinical effect was scored by EULAR criteria, radiographic progression was assessed using Sharp/ van der Heijde (SVH) modified scoring method. B-cell level was measured with flow cytometry.

Results: patients who were treated by different doses of RTX (500 x2 or 1000 x2) had good response. After 48 week of treatment RTX clinical improvement was achieved in 65% pts, good and moderate response by EULAR criteria in 23% and 42% pts respectively. Noteworthy, after 12 months of treatment RTX radiological progression was absent in 50% pts with high disease activity. There was no significant difference in the degree of B-cell reduction when assessing the clinical and antidestructive effects. However, in assessing the clinical effect, it was noted that depletion of B cells in patients with RA in a state of remission (median 0.05% vs 23 % and 42 % pts respectively). Noteworthy, after 12 months of treatment RTX clinical improvement was achieved in 65% pts, good and moderate response by EULAR criteria in 23% and 42% pts respectively. Noteworthy, after 12 months of treatment RTX radiological progression was absent in 50% pts with high disease activity. There was no significant difference in the degree of B-cell reduction when assessing the clinical and antidestructive effects. However, in assessing the clinical effect, it was noted that depletion of B cells in patients with RA in a state of remission (median 0.05% vs 23 % and 42 % pts respectively).

Conclusion: rituximab therapy slows the radiologic progression regardless of the therapeutic effect. Radiologic progression did not show any dependence on the degree of B-cell reduction. The most pronounced depletion of B cells was observed in RA patients in a state of remission.

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