Immunogenicity Differs in Abatacept, Infliximab

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MONT TREMBLANT, QUE. — Abatacept and infliximab exhibit different characteristics in their propensity to elicit autoantibody seroconversion and in their immunogenicity profiles in patients with rheumatoid arthritis, according to findings from a new analysis of data from a multicenter phase III trial.

As with all immunomodulatory agents, the development of autoimmune disorders and the formation of anti–double-stranded DNA (anti-dsDNA) and antinuclear antibody (ANA) is of concern in patients who are being treated with abatacept or infliximab, said Dr. Jacques Brown of le Centre Hospitalier Universitaire de Quebec.

Recombinant biologic agents also have the potential to elicit immunogenicity, and the associated antibodies might mediate drug clearance or prevent its binding to its pharmacologic target.

Moreover, antibodies against anti–tumor necrosis factor therapy have been associated with decreased efficacy and an increased risk of infusion reactions, according to Dr. Brown.

The current analysis investigated 431 patients with rheumatoid arthritis who had an inadequate response to methotrexate. Patients were randomized to receive either abatacept, 10 mg/kg, on days 1, 15, and 29, and every 4 weeks thereafter; or infliximab, 3 mg/kg on days 1, 15, 43, and 85, and every 56 days thereafter for 6 months; or placebo.

Patients' mean age was 49 years and mean disease duration was 8 years. All had active disease, with a mean Disease Activity Score 28 of 6.8, tender joint counts above 30 and swollen joint counts above 20, and poor physical function on the Health Assessment Questionnaire Disability Index.

At baseline, 87% of the patients who were receiving abatacept were rheumatoid-factor positive, as were 85% of those patients who were randomized to the infliximab group.

At 6 months, 2% of the abatacept group, 5% of the placebo group, and 32% of the infliximab group had become ANA positive, whereas 1%, 4%, and 39% of these groups had seroconverted to positivity for anti-dsDNA antibodies, Dr. Brown reported in a poster session at the annual meeting of the Canadian Rheumatology Association.

By 1 year, 7% of patients in the abatacept group and 48% of the infliximab group had become ANA positive, whereas 2% of the abatacept group and 48% of the infliximab group had become anti-dsDNA positive.

The patients initially randomized to placebo were switched to abatacept at 6 months and were not included in this analysis.

During the 6-month double-blind phase of the trial, none of the abatacept-treated patients developed antibodies against the drug, whereas 62% of the infliximab-treated patients had developed anti-infliximab antibodies.

During the double-blind phase, one patient in each group developed an autoimmune disorder.

One patient on abatacept developed vasculitis, one patient receiving placebo developed leukocytoclastic vasculitis, and one patient on infliximab developed sicca syndrome.

By 1 year, one additional patient who originally was randomized to placebo and later was switched to abatacept developed vasculitis.

Infusion reactions, which most commonly consisted of hypotension, headache, and nausea, were seen in 5%, 10%, and 18% of patients in the abatacept, placebo, and infliximab groups, respectively.

By 1 year these reactions were seen in 7% and 25% of the abatacept and infliximab groups.

The profiles of ANA and anti-dsDNA antibodies were markedly different in the two active treatment groups, although this difference did not translate into an increase in autoimmunity, with very few patients developing autoimmune disorders.

Furthermore, because vasculitis and sicca syndrome are associated with rheumatoid arthritis, it is difficult to determine whether the association is with the disease or with the use of biologic agents, Dr. Brown wrote.

The clinical impact of these differences remains to be elucidated, he added.

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