Post-Rituximab Infection Rates Remain Stable

VITALS

Major Finding: Previous treatment with rituximab does not increase infection risk in RA patients who subsequently receive other biologic therapies during the period of peripheral B-cell depletion.

Data Source: A subgroup analysis of patients with moderate to severe RA who received rituximab as part of an international clinical trial program.

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BY DIANA MAHONEY

FROM THE ANNUAL MEETING OF THE CANADIAN RHEUMATOLOGY ASSOCIATION

CANCÚN, MEXICO – The use of other biologic therapies in rheumatoid arthritis patients previously treated with rituximab has been shown to not be associated with an increased risk of serious infection in this population.

"The rate of serious infections [in these patients] is consistent with rates observed in long-term safety analyses of rituximab-treated patients," reported Dr. Mark C. Genovese.

The study was designed to determine whether residual pharmacodynamic effects following discontinuation of rituximab render rheumatoid arthritis patients more vulnerable to serious infection during subsequent biologic treatment.

To make that determination, Dr. Genovese, professor of medicine (immunology and rheumatology) at Stanford (Calif.) University, and his colleagues reviewed the outcomes of patients with moderate to severe

RA who received rituximab and methotrexate in an international clinical trial program and who were subsequently treated with a different biologic during the safety follow-up period.

Of the 3,189 RA patients who had received at least one course of rituximab in the clinical trial, 283 were subsequently treated with an alternative biologic agent during safety follow-up, according to Dr. Genovese.

Of these, 230 patients received tumor necrosis factor (TNF) inhibitors as their first subsequent biologic agent after rituximab.

Another 43 received the T-cell inhibitor abatacept (including 2 who subsequently received a TNF inhibitor), 9 received the interleukin-1 inhibitor anakinra (also including 2 who subsequently received a TNF inhibitor), 3 received the interleukin-6 receptor inhibitor tocilizumab, and 2 received experimental biologic agents.

Despite its peripheral B-cell depletion, rituximab does not up infection rates with subsequent biologics.

DR. GENOVESE

The median time from the last dose of rituximab to the first subsequent biologic was 8 months (mean 10 months), he reported. The average follow-up time after receiving the subsequent biologic was 11 months.

The investigators collected information on "serious infection events," defined as infections that required intravenous antibiotics or met the regulatory criteria for a serious adverse event, including infections that required inpatient hospitalization; were immediately life-threatening; were medically significant and required an intervention to prevent one of the previous outcomes; or were fatal.

They calculated the rates of such events for the periods in which patients were on rituximab before the subsequent biologic and after initiation of treatment with the subsequent biologic, Dr. Genovese said.

They also collected peripheral CD19+ counts, which are a surrogate marker for CD20+ B cells.

Following the first dose of rituximab and prior to subsequent biologic therapy, 22 serious infections in 18 patients over 366 patient-years of follow-up (6 events/100 patient-years) were reported. "The infections were variable and typical of RA patients, and did not include any opportunistic or fatal infections," Dr. Genovese said.

At the time of receiving subsequent biologic treatment, 83% of the patients had peripheral B-cell counts below the lower limit of normal, he noted.

After treatment with another biologic following rituximab, a total of 16 serious infection events – also variable and typical of RA – occurred in 15 patients over 321,64 patient-years of follow-up (5 events/100 patient-years).

The median time to infection after initiating the subsequent biologic was 11 months, he said.

Of the 16 serious infection events, 12 occurred in patients who had received TNF inhibitors as their first post-rituximab biologic, and 4 occurred in patients who had received two biologic drugs post rituximab, said Dr. Genovese.

One serious infection was reported before alternative treatment and one after treatment among the 43 patients who received abatacept, according to Dr. Genovese.

In the subgroup of patients who received a TNF inhibitor following rituximab, the serious infection rates before and after receipt of the drug were 6.03/100 patient-years and 4.51/100 patient-years, respectively.

Overall, the serious infection rates in the 283 patients were statistically similar to the rate of 4.35 events/100 patient-years observed in the all-exposure safety population, according to Dr. Genovese's presentation.

In the subgroup of patients with CD19+ cell counts of less than 20 cells/mcL prior to subsequent biologic treatment, the serious infection rate, found to be at 6 events/100 patient-years, was also consistent with the serious infection rates observed in all patients who were receiving any biologic disease-modifying antirheumatic drug following rituximab, he said.

"The findings answer an important clinical question about the safety of treatment with other biologic drugs during the period of peripheral B-cell depletion in patients who have discontinued rituximab," Dr. Genovese concluded. ■

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