Tofacitinib Improves Disease Control in Rheumatoid Arthritis

Tofacitinib improves disease control and slows disease progression in rheumatoid arthritis more effectively than methotrexate in a phase 3 trial.

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January 25, 2016 – Tofacitinib reduced the signs and symptoms of rheumatoid arthritis and slowed radiographic disease progression more effectively than methotrexate, a phase 3 study showed.

Dr. Eun Bong Lee, MD, with Seoul National University College of Medicine in Seoul, South Korea, and the ORAL Start Investigators reported their findings in the June 19, 2014 issue of the New England Journal of Medicine.

Tofacitinib is an oral Janus kinase inhibitor that has been shown to improve disease control in and reduce disability due to rheumatoid arthritis in phase 3 trials. To date, tofacitinib has not yet been studied as an alternative to methotrexate, which as monotherapy is associated with significant side effects that may lead to high rates of drug discontinuation. However, safety concerns have been raised regarding tofacitinib as well, including serious infection and elevated low-density lipoprotein levels. This study compared the efficacy and safety of tofacitinib with methotrexate in patients with moderate-to-severe rheumatoid arthritis who have not previously received methotrexate.

A total of 958 patients were randomized in a 2:2:1 ratio to receive tofacitinib 5 mg twice a day; tofacitinib 10 mg twice a day; or methotrexate 10 mg per week for 4 weeks, then 15 mg per week for 4 weeks, then 20 mg per week thereafter. However, only 956 patients received study drug as 2 patients were randomized but not treated.

To assess disease control and progression, investigators used as primary endpoints American College of Rheumatology (ACR) 70 (at least a 70% reduction in the number of both tender and swollen joints and improvement in three of five other criteria) response and change in the van der Heijde modification of the total Sharp score (ranging from 0 to 448 points; higher scores correspond to greater structural joint damage).

At 6 months, significantly more patients receiving tofacitinib 5 mg and tofacitinib 10 mg had an ACR 70 response compared with those receiving methotrexate (25.5% and 37.7% vs 12.0%, P < .001 for both comparisons). Changes in the modified total Sharp score were modest in all groups but were significantly smaller in the 5-mg and 10-mg tofacitinib groups (0.2 points and <0.1 point vs 0.8 points in the methotrexate group, P < .001 for both comparisons). Similar findings were maintained at 12 and 24 months.

Infection was the most common serious adverse event. Herpes zoster infections occurred more frequently in patients receiving 5 mg or 10 mg of tofacitinib (3.5% and 4.5% vs 1.1% of patients receiving methotrexate). Investigators confirmed 5 cases of malignancy in the tofacitinib groups and 1 case in the methotrexate group. The rate of elevated low-density lipoprotein levels was higher in patients receiving tofacitinib. However, the proportion of patients who discontinued study drug due to adverse events was similar among the 5-mg and 10-mg tofacitinib groups and the methotrexate group (10.7%, 10.3%, and 13.4%, respectively).

Dr. Lee and colleagues concluded that tofacitinib “can be more effective clinically, functionally, and radiographically than methotrexate in patients with rheumatoid arthritis who have not previously received methotrexate.” However, because this study included only patients with moderate-to-severe disease, the results cannot be generalized to patients in the early stages of rheumatoid arthritis. They also noted that while tofacitinib is the only disease-modifying antirheumatic drug shown to be superior to methotrexate, “[the] benefits of tofacitinib need to be considered in the context of the risks of adverse events.”
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