Baricitinib Tied to Symptom Reduction in Refractory Rheumatoid Arthritis

Baricitinib, a tyrosine kinase inhibitor, reduces symptoms in patients suffering from refractory rheumatoid arthritis.

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April 18, 2016 – An oral Janus tyrosine kinase (JAK) inhibitor, baricitinib, alleviates rheumatoid arthritis symptoms in patients who are nonresponsive to traditional disease-modifying antirheumatic drugs (DMARDs), a new phase 3 study reports.

The research out of the Stanford University Medical Center led by Mark C. Genovese, M.D. was published in *The New England Journal of Medicine* on March 31, 2016.

In patients with rheumatoid arthritis, circulating cytokines bind JAK receptors on the cell surface, initiating a signal cascade implicated in autoimmune inflammation. Baricitinib specifically inhibits JAK1 and JAK2 receptors and appears to reduce joint inflammation in patients who are nonresponsive to traditional DMARDs or have unacceptable side effects. Approximately 20% of rheumatoid arthritis patients fall into this category. In the present study, researchers evaluated the efficacy of baricitinib in refractory patients in a randomized, multisite phase 3 clinical trial.

Patients with moderate to severe rheumatoid arthritis were randomized 1:1:1 to three groups receiving 2 mg baricitinib, 4 mg baricitinib, or placebo over the 24-week trial period. There were multiple trial end points, including the American College of Rheumatology 20% (ACR20), the 28-joint disease activity score based on C-reactive protein level (DAS28-CRP), the Health Assessment Questionnaire–Disability Index (HAQ-DI), and a simplified activity index (SDAI) of 3.3 or less.

In the 4-mg treatment group, the researchers saw a significant improvement in the primary end point of the trial, the ACR20 (55% vs. 27%, baricitinib vs. placebo, $P < .001$). Furthermore, there were improvements in two of the three secondary end points, the HAQ-DI ($P < .001$) and DAS28-CRP ($P < 0.001$), but there was no significant difference between placebo and 4-mg baricitinib treatment in the SDAI ($P = 0.14$).

The researchers divided the study sample into subgroups based on the number of prior biological DMARDs, tumor necrosis factor inhibitors, and non-tumor necrosis factor inhibitor DMARDs prescribed. Baricitinib (4 mg) had a significant effect in all of these subgroups, indicating that the drug is effective in a variety of types of refractory rheumatoid arthritis and in patients who have tried an assortment of pharmacological interventions.

Adverse effects of baricitinib treatment included herpes zoster infections (4% vs. 1% vs. 1% in 4-mg vs. 2-mg vs. placebo groups) and increased neutrophil count ($P < .001$), creatinine levels ($P < .001$), and cholesterol ($P < .001$). Additionally, one death occurred in the 4-mg baricitinib group. A 76-year-old patient with preexisting diabetes mellitus died as a result of basilar-artery thrombosis. This was one of two serious cardiovascular events observed during the study, the second of which also occurred in a patient with

preexisting diabetes mellitus in the 4-mg baricitinib group. The rates of serious adverse events were similar in the placebo and treatment groups.

“This is the first drug to demonstrate meaningful clinical benefit in patients who’ve failed virtually every other commercial drug for rheumatoid arthritis,” Dr. Genovese noted in a press release out of Stanford University. “It’s an ever-growing population,” he adds.

This study was sponsored by Eli Lilly and Incite.

The New England Journal of Medicine. Published March 31, 2016.