

# Two Interleukin Antibodies on the RA Horizon

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AMSTERDAM — Efforts to broaden the spectrum of biologic agents available for use in the treatment of rheumatoid arthritis continue, with early studies suggesting possible eventual roles for antibodies targeting two interleukins.

In a phase II study, the safety and efficacy of a human monoclonal antibody to IL-15 (AMG 714) were evaluated in 180 pa-

tients who had active rheumatoid arthritis (RA) and had failed at least one disease-modifying antirheumatic drug but who had not previously received any biologic intervention, Dr. Ian McInnes said at the annual European Congress of Rheumatology.

An initial group of 110 patients were randomized to receive the anti-IL-15 antibody in doses of 40, 80, 160, or 280 mg or placebo by subcutaneous infusion. Following a protocol amendment, an additional 70 patients were randomized to re-

ceive 280 mg or placebo every 2 weeks for 12 weeks. Efficacy was evaluated in the 114 patients who received the highest dose or placebo, with the primary end point being the proportion of patients achieving an American College of Rheumatology (ACR) 20 response at week 14.

A significantly greater number of patients receiving 280 mg of AMG 714 achieved an ACR 20 response than did those receiving placebo at week 12 (64% vs. 34%, respectively) and at week 16 (66%

vs. 38%), said Dr. McInnes of the Glasgow (Scotland) Royal Infirmary.

At week 14, however, ACR 20 was achieved by 54% of the active treatment group and 38% of the placebo group, which was not a statistically significant difference.

Levels of acute phase reactants decreased significantly in the 280-mg group, compared with those on placebo, with C-reactive protein (CRP) levels remaining 50%-67% lower than in the placebo group throughout the study. "These data demonstrate pharmacologic activity of AMG 714 as indicated by the reduction of acute phase reactant levels," Dr. McInnes said.

Serious infections were reported by one patient in the 80-mg active treatment group (sepsis) and by one patient in the placebo group (viral bronchitis).

Dr. McInnes said that although the primary efficacy end point was not met, the overall clinical results suggest that inhibiting IL-15 with this antibody may be an important treatment strategy for RA and other inflammatory conditions.

In another phase I/II proof-of-concept study conducted in 13 centers in Germany, the Netherlands, and Switzerland, the fully human anti-IL-1 $\beta$  monoclonal antibody ACZ885 was evaluated in 53 patients with active rheumatoid arthritis, Dr. Rieke Alten said at the meeting, sponsored by the European League Against Rheumatism.

All patients had more than six tender joints, six swollen joints, and CRP levels greater than 0.6 mg/dL or an erythrocyte sedimentation rate greater than 28 mm/h despite optimal doses of methotrexate (7.5-25 mg/week) for at least 10-12 weeks.

They were randomized to receive placebo or 0.3, 1, 3, or 10 mg/kg of the anti-IL-1 $\beta$  antibody, which was administered as a 2-hour intravenous infusion on days 1 and 15. Although the main objective of the study was to evaluate the pharmacokinetics and pharmacodynamics of the drug, a larger number of patients were included in the 10 mg/kg group so that some initial data on efficacy could be obtained, according to Dr. Alten of Schlosspark-Klinik, Berlin, Germany.

In the 3-mg group, 4 of 6 patients (67%) achieved ACR 20 responses, as did 6 of 19 (32%) in the 10-mg group.

In addition, in the 10-mg group, three patients (16%) and two patients (11%) reached ACR 50 and 70 responses, respectively, Dr. Alten said.

These were "important clinical improvements," he said.

Decreases in CRP levels occurred within 1-2 weeks in all dose groups, and the duration of CRP suppression was dose dependent. No human antihuman antibodies developed on follow-up through day 112, and there were no changes in pharmacokinetics that would suggest the development of anti-ACZ885 antibodies, he said.

The infusions were well tolerated, and there were no drug-related laboratory abnormalities. Infections were limited to one case of erysipelas and one of pneumonia, both of which resolved with standard antibiotic therapy.

Studies to determine an optimal dosing regimen and characterize clinical effects in RA are warranted, Dr. Alten concluded. ■



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