IL-17A Blocker Shows Early Promise for Psoriasis

BY BRUCE JANCIN

BERLIN — Selective inhibition of the proinflammatory cytokine interleukin-17A using a novel fully human monoclonal antibody showed considerable early promise for treatment of psoriasis in a phase II double-blind randomized trial.

This was a proof-of-concept study, and what it proved is that the interleukin 17A–producing T helper 17 cells are an entirely new and attractive therapeutic target in moderate to severe chronic plaque psoriasis, Dr. Zoe Draelos reported at the annual congress of the European Academy of Dermatology and Venereology.

Based upon the phase II results, it's full speed ahead for development of the fully human IgG monoclonal antibody known for now as AIN457. The next round of clinical trials will be considerably larger, longer term, and aimed at identifying optimal dosing, according to Dr. Draelos, a dermatologist in High Point, N.C.

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DR. DRAELOS

AIN457 is also in clinical trials for the treatment of other immune-mediated disorders, most notably rheumatoid arthritis and noninfectious uveitis. It is also being studied for the treatment of Chrohn's disease.

The phase II study involved 36 patients with chronic plaque psoriasis covering at least 10% of their body surface area and an Investigator's Global Assessment (IGA) severity score of 3 or more, according to Dr. Draelos.

Participants were randomized to a single intravenous infusion of AIN457 at 3 mg/kg or placebo and then followed for 12 weeks.

The study had two primary end points: change in Psoriasis Area and Severity Index (PASI) score at 4 weeks and reduction in IGA score.

The mean decrease in PASI score 4 weeks after the infusion was 58% in the AIN457-treated patients and 4% with placebo, she said.

The response was fast, with a significant difference from placebo emerging within 2 weeks of infusion.

At 12 weeks, the mean reduction in PASI was 63% in patients who received the IL-17A blocker and 9% in controls. A 50% decrease in PASI score (PASI 50) was recorded by 72% of AIN457-treated patients, a PASI 75 by 44%, and a PASI 90 by 11%.

Eighty-three percent of AIN457-treated patients had at least a one-point improvement in IGA score at week 4, compared with 11% of controls. By week 12, 28% of patients in the active-treatment arm had an IGA score of 1, indicative of being almost clear, compared with 6% of controls.

AIN457 exhibited a favorable side effect profile in this small study. No serious adverse events were attributed to the study drug.

Five AIN457-treated patients and three controls developed sinusitis or another infection during the follow-up period. Importantly, no one who received AIN457 developed anti-AIN457 antibodies.

IL-17A, which is upregulated in psoriatic lesional skin, has been called the master regulator of innate defense protein synthesis in keratinocytes.

Dr. Thomas A. Luger, president of the EADV congress, who wasn't involved in the AIN457 study, singled it out as a highlight of the meeting.

"I think this is exciting. It's early data, but it is proof of the concept that this antibody offers a new way to treat psoriasis," said Dr. Luger, professor and chair of the department of dermatology at the University of Münster (Germany).

Other anti-IL-17A antibodies are also in the developmental pipeline, but AIN457 is furthest along, he noted.

The phase II trial for AIN457 was funded by Novartis. ■