Editorial

Tipping the Scales: Biologic Therapy 2002

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We welcome our annual psoriasis issue with a sense of anticipation as the new biologics for psoriasis continue to be investigated and as the first medication in this class nears approval by the US Food and Drug Administration (FDA). I want to provide an update on the progress of the "big 4" biologic agents.

Alefacept

An international multicenter trial randomized more than 500 patients to 1 of 3 arms: intramuscular (IM) alefacept 15 mg once a week for 12 weeks, IM alefacept 10 mg once a week for 12 weeks, or placebo. Two weeks after the last dose was given, 21% of patients treated with the 15-mg dose achieved at least a 75% reduction from baseline in their Psoriasis Area and Severity Index (PASI) score compared with 5% of patients receiving placebo ($P<.001$).[1]

The FDA will review the marketing application for alefacept within 6 months. An early 2003 approval of the drug is anticipated.

Etanercept

A second, global phase 3 pivotal study assessing the efficacy and tolerability of etanercept to treat moderate to severe plaque psoriasis was initiated this year. In addition, phase 2 study results on psoriasis patients were released. In this phase 2 clinical study, 112 patients with moderate to severe plaque psoriasis were randomized evenly to receive 25 mg of etanercept or placebo subcutaneously twice a week for 6 months. The primary end point of the study was the proportion of patients achieving a PASI reduction of at least 75% after 12 weeks.[2]

Patients treated with etanercept monotherapy experienced continued improvement throughout the study. At 3 months, 30% of 57 patients on etanercept achieved a 75% reduction in PASI, compared with 2% of 55 patients on placebo ($P<.0001$). Fifty-six percent of patients treated with etanercept achieved a 75% reduction in PASI at 6 months compared with 5% of patients receiving placebo. Additionally, at 6 months 21% of patients receiving etanercept achieved a 90% reduction in PASI compared with none of those patients who received placebo, while 77% of patients receiving etanercept achieved a 50% reduction in PASI compared with 13% of patients receiving placebo. Side effects seen statistically more frequently in patients receiving etanercept in this study were limited to mild infections and injection site reactions. Most observed infections were mild upper respiratory infections and sinusitis. The overall tolerability profile in patients receiving etanercept was similar to that in the placebo group.[2]

Efalizumab

A phase 3 trial with subcutaneous efalizumab, an anti-CD11a agent, showed promising results in treatment of moderate to severe plaque psoriasis. In one study in which efalizumab was evaluated, results after 12 weeks of treatment with either low-dose (1.0 mg/kg per week) or high-dose efalizumab (2.0 mg/kg per week) showed that the PASI score had improved by at least 75% in close to 40% of patients in the low-dose group and in approximately 25% of the high-dose group.[3] More than 60% of patients who received the 1.0 mg/kg per week dose and more than 50% of those who received 2.0 mg/kg per week achieved improvement in PASI score of at least 50% compared with baseline. Some 15% of those who were treated with placebo achieved a similar improvement.[3]

Infliximab

Schopf and colleagues[4] in Mainz, Germany, treated 8 patients with severe psoriasis in an open-label trial with infliximab 5 mg/kg. They infused infliximab 5 mg/kg at weeks 0, 2, and 6 and evaluated changes such as PASI score, pruritus severity, and epidermal thickness. Between weeks 0 and 10, they documented a nearly 85% reduction in mean PASI score; while at week 14, 2 months after patients had

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received the last infliximab dose, the mean PASI score was dramatically reduced by 67% from baseline. Pruritus was significantly reduced ($P<.01$) from baseline at weeks 2 through 14, with mean epidermal thickness significantly normalized from 0.41 mm at week 0 to 0.14 mm at week 10. Importantly, laboratory assessments remained normal during the treatment course.

The data on these new therapies is very encouraging, but much work remains to be done. Hopefully the next year will continue to bring us favorable reports regarding the safety and efficacy of these new therapies.

REFERENCES

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