

Psoriasis Poses Independent Risk for Heart Disease

BY DAMIAN McNAMARA

Miami Bureau

MONTREAL — Psoriasis is an independent risk factor for increased cardiovascular morbidity and mortality, according to a growing number of studies and new guidelines from the American Academy of Dermatology.

Based on this evidence, it is important to screen and regularly monitor psoriasis patients for cardiovascular disease risk factors, said Dr. Lyn C. Guenther, professor and chair of the division of dermatology at the University of Western Ontario, London.

An increased prevalence of cardiovascular disease among people with psoriasis—especially more severe forms—is not new. “I thought it was all related to their [increased] weight,” Dr. Guenther said. “Psoriasis appears to be an independent risk factor now.”

The American Academy of Dermatology addressed increased cardiovascular risk among people with psoriasis in guidelines released in May (“New Psoriasis Guidelines Emphasize Biologics,” SKIN & ALLERGY NEWS, July 2008, p. 17). Studies also have suggested an increased prevalence of hypertension and diabetes in people with psoriasis (J. Am. Acad. Derm. 2006;55:829-35) contributes to the risk, as does a typically atherogenic lipoprotein profile at the onset of skin disease (J. Am. Acad. Dermatol. 2007;56:629-34).

“This is something we cannot ignore any longer,” Dr. Guenther said during a symposium sponsored by Abbott

at the annual conference of the Canadian Dermatology Association. “I am not necessarily suggesting we are the ones who have to address this, but [we should] make sure these comorbidities are addressed.”

Psoriasis is associated not only with increased cardiovascular morbidity, but increased mortality. “This theme comes up repeatedly,” said Dr. Guenther, who has worked as a researcher, consultant, and speaker for Abbott, Amgen/Wyeth, Schering Plough, Astellas, and Leo Pharma.

People with severe psoriasis have a 50% increased risk of death and tend to die earlier than do those without psoriasis (males 3.5 years earlier, females 4.4 years earlier). These figures do not apply to mild disease, she emphasized.

Not surprisingly, people with psoriasis also have an increased prevalence of metabolic syndrome, Dr. Guenther said. In one case-control study, 30% of 338 adults with chronic plaque psoriasis and 21% of 334 adults with other skin diseases met criteria for metabolic syndrome—a difference that was statistically significant (Br. J. Dermatol. 2007;157:68-73).

In addition, younger patients with more severe psoriasis appear to be the group at greatest relative risk for a myocardial infarction (JAMA 2006;296:1735-41). Those with severe psoriasis at age 30 years had more than three times the risk (relative risk, 3.1) of having a myocardial infarction, compared with the general population. Risk was lower but still elevated for 30-year-olds with mild psoriasis (RR, 1.29). In 60-year-olds, however, severe psoriasis conferred a 1.36 relative risk for an MI and mild psoriasis conferred a 1.08 relative risk.

Inflammation may be the common culprit in both psoriasis and increased cardiovascular disease. “Tumor necrosis factor- α [TNF- α] is involved in cardiovascular disease and is a target for many of our therapies. High TNF levels are an independent predictor of cardiovascular morbidity and mortality, and TNF levels are high in psoriasis,” Dr. Guenther said.

Elevated C-reactive protein levels may be an important link between psoriasis and cardiovascular disease as well, as was suggested in an editors’ roundtable in the American Journal of Cardiology (Am. J. Cardiol. 2008;101:1119-26). “C-reactive protein is something we are starting to measure in our patients,” said Dr. Guenther, who called the marker a very sensitive indicator of inflammation.

There are also immunologic similarities between atherosclerosis and psoriasis. Cell activation, inactive immunity, and adaptive immunity indicate that pathogenesis is similar between these two diseases, she said.

The good news is that treatment of psoriasis might reduce cardiovascular disease and death. “It makes sense that if you reduce inflammation, CRP, and TNF, it might reduce cardiovascular morbidity and mortality,” Dr. Guenther said. ■

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psoriasis news
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Talarozole Shows Promise for Moderate to Severe Psoriasis

KYOTO, JAPAN — The novel oral drug talarozole proved safe and effective for treatment of moderate to severe plaque psoriasis in a 176-patient multicenter phase IIb clinical trial.

On the basis of the dose-response pattern noted in the study, the once-daily 2-mg dose has been selected for further development in pivotal phase III studies, Dr. Christopher E.M. Griffiths said at an international investigative dermatology meeting.

Talarozole (Rambazole) is not a retinoid. Rather, this investigational triazole derivative increases intracellular levels of endogenous retinoic acid by inhibiting cytochrome P450-dependent catabolism of all-trans retinoic acid, said Dr. Griffiths, professor of dermatology and head of the Research School of Translational Medicine at the University of Manchester (England).

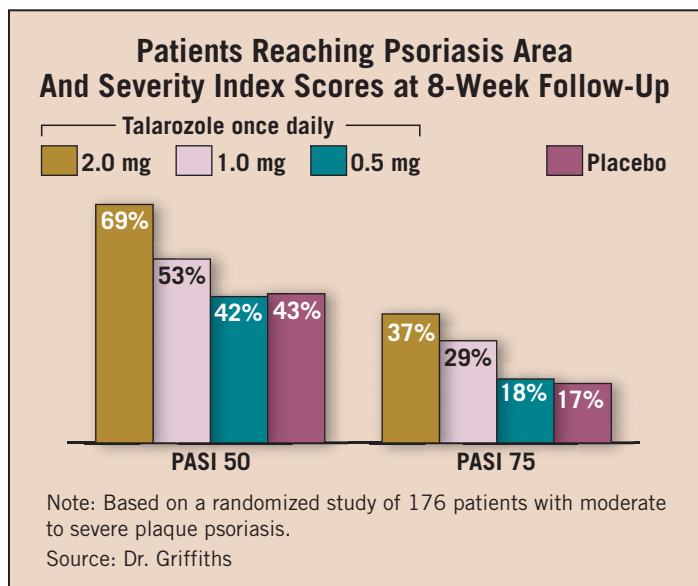
Participants in the phase IIb trial were randomized to 12 weeks of placebo or to 0.5, 1.0, or 2.0 mg of talarozole once daily. Clinical improvement at 20 weeks—8 weeks after treatment cessation—was greatest in the 2-mg group (see chart). Psoriasis Area and Severity Index scores

indicative of 50% and 75% improvement continued to fall after treatment ended; further studies will examine the duration of this effect, he said at the meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

Safety monitoring included serial ECGs, psychiatric evaluations for depression, ophthalmologic and auditory testing, and clinical laboratory tests. Adverse events were mild to moderate, transient, and less pronounced than typical with exogenous retinoid therapy, said Dr. Griffiths.

Barrier Therapeutics, which sponsored the trial, also has a topical version of Rambazole in phase IIa studies for the treatment of acne.

—Bruce Jancin



Acitretin-Etanercept Combo Beneficial in Plaque Psoriasis

BY BRUCE JANCIN

Denver Bureau

KYOTO, JAPAN — Combining once-weekly etanercept with daily acitretin is as effective as standard full-dose, twice-weekly etanercept monotherapy in the treatment of moderate to severe chronic plaque psoriasis, according to the first randomized trial of a combined biologic/nonbiologic regimen in treating the disease.

“The low dose of etanercept used in this combination could significantly reduce the cost of treatment,” Dr. Micol Del Giglio observed at an international investigative dermatology meeting. The combination addresses both the tumor necrosis factor- α -mediated immune aspect of psoriasis and the disease’s hyperproliferative dimension, Dr. Micol Del Giglio said at an international investigative dermatology meeting.

He reported on 60 adults with moderate to severe chronic plaque psoriasis who participated in an investigator-initiated and investigator-blinded, 24-week clinical trial.

Subjects were randomized to subcutaneous etanercept in the standard regimen of 25 mg administered subcutaneously twice per week, oral acitretin at 0.4 mg/kg per day, or the combination of etanercept at 25 mg once weekly plus acitretin at 0.4 mg/kg per day.

The primary study end point was a 75% or greater improvement in Psoriasis Area and Severity Index (PASI) scores at week 24, compared with baseline.

This value was achieved in 45% of patients in the standard-dose etanercept

group, in an identical percentage of those in the combined treatment arm, and in 28% of the acitretin-only group. The difference in outcome between the two etanercept-based treatments and acitretin was significant, said Dr. Del Giglio of the University of Verona (Italy).

A 50% or greater improvement in PASI scores was documented in 70% of patients on the acitretin/low-dose etanercept combination, 70% in those on full-dose etanercept, and 50% on acitretin, he reported.

The safety profiles of the three regimens over 24 weeks were similar. Particularly noteworthy was the fact that the combined regimen was not associated with significant changes in liver enzymes, total cholesterol, or triglycerides, Dr. Del Giglio noted at the meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

He added that future studies should look at whether combining daily acitretin with biweekly etanercept also results in the sort of efficacy expected of a potent biologic therapy. Quality of life assessments should be incorporated, as less frequent etanercept dosing may result in fewer biologic side effects.

“The combination could be used from the beginning, as shown in this study, or alternatively etanercept could be added to acitretin in patients not adequately controlled on the latter,” the dermatologist said.

Dr. Del Giglio disclosed no financial conflicts of interest with regard to this study. ■