Kaposi's Sarcoma Advances Include New Gel, PDT, More

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VANCOUVER, BC--Discussions of Kaposi's sarcoma at the 11th International Conference on AIDS included reports on a promising topical treatment, photodynamic therapy (PDT), a chemotherapy regimen that could save up to $1,000 per course, and the possibility of prevention using antitherpes drugs.

A retinoid gel shows promise of becoming the first topical therapy for Kaposi's sarcoma (KS), said Madeleine Duvic, MD, chief, Dermatology Section, University of Texas M.D. Anderson Cancer Center. In a phase I/II clinical trial, the 9-cis-retinoic acid (ALRT 1057, being developed by Ligand Pharmaceuticals Inc., San Diego) proved safe and well tolerated. And although the trials was not designed to evaluate efficacy, the researchers found that the gel produced complete resolution of lesions in 9% of patients and resolution of at least half of lesions in 23%.

Importantly, responses were seen in patients with a wide range of CD4 counts, including four patients with counts below 50 cells/mm3. Dr. Duvic suggested that the retinoid gel may make possible a form of "patient-controlled, conservative management" in the early phases of KS. This multicenter study enrolled 63 patients with biopsy proven, multiple KS lesions. Patients applied the gel to selected index lesions one to four times daily. Similar control lesions were left untreated (but could be treated after 8 to 16 weeks). Forty-three patients with 179 treated index lesions and 119 control lesions received at least 12 weeks of therapy (or had withdrawn prior to 12 weeks).

Response in KS lesions has been notoriously hard to evaluate because the area of pigmentation associated with the lesion may not shrink even though response is demonstrable histopathologically, Dr. Duvic said. This study used methodology developed by the AIDS Clinical Trials Group, to evaluate response by measuring area and elevation of the lesion.

Partial responses for treated lesions occurred in 13 patients (30%) vs 4 (9%) for control lesions. A complete flattening of at least 50% of raised lesions was achieved in 26% of the treated group vs 9% in the control group, and a 50% or greater decrease in the sum of the area of lesions occurred in 7% of the treated group but in none of the control group.

"One or more lesions responded in 30% of patients," Dr. Duvic said. Responses were sustained for a median follow-up of 16 weeks; only 4 of 28 lesions had relapsed after a median of 12 weeks.

Photodynamic therapy with the investigational agent tin ethyl etiopurpurin (SnET2, being developed by PDT, Inc., Santa Barbara, Calif) had a positive effect on KS skin lesions, particularly papular stage KS, in studies at the U. of California, San Francisco, said Roy Grekin, MD, chief of dermatologic surgery.

In these phase I/II clinical trials, Dr. Grekin and his colleagues treated 29 patients with 172 skin lesions using various drug and light combinations. They found that a therapeutic dose of SnET2 at 1.2 mg/kg with light irradiation at 300 J/cm² produced a response rate of 87% among papular stage KS lesions and 41% among macular stage KS lesions.

UCSF is now participating in PDT, Inc.'s multicenter phase II/III pivotal clinical trials of photodynamic therapy for KS, which started last March.

Although the drug cost of treatment with DaunoXome (liposomal daunorubicin) for advanced HIV-associated KS is slightly higher than that of the standard three-drug ABV regimen (Adriamycin, bleomycin, vincristine), the total cost to administer a standard course of therapy is approximately 10% less for Dauno-Xome, Gale E. Savage, MD, said at the AIDS conference. The savings per course of treatment (eight cycles over 16 weeks) came to $974.
Less Expensive to Administer

The pharmacoeconomic analysis by Dr. Savage, clinical manager in health economics with S&FA, Inc., in Alexandria, Virginia, included the costs of the chemotherapy drugs, drug administration, monitoring costs, and managing side effects.

Using this four-factor model and data from the pivotal phase III clinical trial of DaunoXome, Dr. Savage found that DaunoXome, because it is a single therapy as opposed to combined therapy, was less than half as expensive to administer as ABV therapy. Although some Dauno-Xome patients required more growth factors, this cost was more than offset by a drop in the costs associated with monitoring for side effects, Dr. Savage said.

The discovery in 1994 that a herpesvirus (known as human herpesvirus-8, HHV8, or KS-associated herpesvirus, KSHV) is involved in causing HIV-related KS immediately raised the question of possible prevention using currently available antiherspes drugs.

This approach has now been studied retrospectively by the Royal Free Hospital and Westminster Hospitals Collaborative Group, London. "Both foscarnet and ganciclovir may have some activity in preventing the occurrence of Kaposi's sarcoma," Amanda Mocroft, MSc, said at the conference.

The London investigators assessed the association between treatment with acyclovir (Zovirax), foscarnet (Foscavir), and ganciclovir (Cytovene) and risk of KS in 3,688 patients with HIV followed for a median of 4.2 years.

Sixteen percent of patients (598) developed KS during the 4-year period. The risk of developing KS was significantly lower in patients who had been treated with foscarnet or ganciclovir. Risk was not decreased by treatment with acyclovir.

The lower risk of developing KS associated with foscarnet or ganciclovir treatment remained after the researchers adjusted for gender, exposure category, age, antiretroviral treatment, PCP prophylaxis, CD4 count, and development of AIDS-defining conditions, including a separate adjustment for the development of cytomegalovirus or herpes simplex, Ms. Mocroft said. "Further studies of the antiviral effect of these drugs are clearly warranted," she concluded.

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