INTRODUCTION

It is difficult to treat Kaposi's sarcoma by conventional therapies in the setting of immune deficiency such as the acquired immunodeficiency syndrome (AIDS), because this treatment may cause further immune suppression. In AIDS, cytotoxic chemotherapy may, for example, increase the risk of opportunistic infections such as Pneumocystis pneumonia. Thus, this therapy, even if successful against the tumor, may potentially shorten survival. Because of these factors, experimental therapy with immune modulating agents has been particularly attractive in AIDS-related Kaposi's sarcoma. The two agents receiving most attention have been recombinant alpha interferon and recombinant interleukin-2. These will be the subject of this review. The results will be preliminary because the disease itself is so new and because many of the clinical trials of these agents are still in progress.

KAPOSI'S SARCOMA - CLINICAL PERSPECTIVES

Kaposi's sarcoma itself is not a new disease. Prior to AIDS, the principal affected populations in the United States were elderly men of Jewish or Mediterranean descent or patients with exogenous immunosuppression especially following renal transplantation(1,2). While Kaposi's sarcoma in AIDS is histologically indistinguishable from other settings, its clinical course is unique. While Kaposi's sarcoma in the elderly usually remains confined to the skin of the lower extremities and follows a relatively indolent course, the same tumor in AIDS is characterized by widespread cutaneous and visceral dissemination, rapid progression and early mortality either as a direct result of the tumor or from opportunistic infections associated with the underlying immunodeficiency(3).

No generally useful staging system for AIDS-related KS has been developed, but reports suggest that those clinical
features which suggest more advanced immune deterioration are associated with a poor prognosis in patients with Kaposi's sarcoma(4,5).Principal among these are the presence of associated lymphoma-like B symptoms (unexplained night sweats, fevers, and weight loss) as well as elevations of the erythrocyte sedimentation rate, neutropenia or severe anemia.

THERAPY OF KAPOSI'S SARCOMA PRIOR TO AIDS

Traditional Kaposi's sarcoma has been responsive to several chemotherapeutic agents, especially vinca alkaloids. Therapy for Kaposi's sarcoma in African populations prior to AIDS has also resulted in a dramatic response to many cytotoxic agents(6).

A group of patients with Kaposi's sarcoma prior to AIDS which is of great interest for the current epidemic are those patients with tumor following renal transplantation and exogenous immunosuppression. A variety of reports confirm the high rate of Kaposi's sarcoma following renal transplantation(7,8) and further demonstrate an often dramatic tumor regression following discontinuation of these immunosuppressive medications. For these reasons, it is widely believed that if therapies could be developed to restore the relative immune competence in patients with AIDS, that this would be sufficient to control further progression or cause actual tumor regression. Of drugs available with immune modulatory possibilities, two that have received the broadest clinical application are recombinant alpha interferon and recombinant interleukin-2.

CLINICAL TRIALS OF RECOMBINANT ALPHA-INTERFERON

Alpha-interferon is an attractive agent to apply to AIDS-associated Kaposi's sarcoma for several reasons. Among these are its antiviral actions, its immune modulating activity, and its antiproliferative capability(9). The antiviral actions of alpha-interferon, while incompletely studied with respect to the causative AIDS retrovirus, provide a rationale for applications in AIDS. Similarly, the immune stimulating and antiproliferative activities also provide a rationale for this drug for a rapidly progressing tumor such as Kaposi's sarcoma appearing in the setting of immune deficiencies.

Clinical trials with alpha-interferon in AIDS-related Kaposi's sarcoma have been undertaken by numerous investigators. While some trials have used non-recombinant drug, more recent studies have focused on recombinant human alpha-interferon.

Clinical trials of recombinant human alpha-interferon (Schering Corporation) were begun in collaboration with the University of California, San Francisco, and the University of California, Los Angeles, in 1982. In the first trial, 10 patients from each institution were randomized to receive either a low or high dose of this drug. The low dose arm consisted of one million units alpha-interferon per meter square body surface area. It was administered subcutaneously.