Triple therapy regime puts patients with leukemic form of cutaneous lymphoma in remission

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A three-pronged immunotherapy approach nearly doubles five-year survival among patients with rare leukemic form of cutaneous T-cell lymphoma, reports a new study by dermatologists from the Abramson Cancer Center and Perelman School of Medicine at the University of Pennsylvania.

In a retrospective study of 98 patients with advanced Sezary Syndrome – treated over a 25 year time span at the Hospital of the University of Pennsylvania – patients treated with combination therapy experienced a higher overall response rate compared to previous studies (74.4 percent vs. 63 percent), and a higher complete response rate (30 percent vs. 20 percent). The 5-year overall survival rate was also higher than previously reported (55 percent vs. 30 percent). Researchers concluded that combination immunotherapy is more effective than a single treatment.

"This rare disease, if caught soon enough, may no longer be fatal, thanks to advances in treatment and our understanding of the disease," said Alain Rook, MD, professor of Dermatology and senior author of the study, which appears online in the *Archives of Dermatology*. "In addition, our improved understanding of prognostic factors will help us tailor treatments for each patient, based on the aggressiveness of their disease, and better predict individual patient outcomes."

Sezary Syndrome is difficult to treat and has had a poor prognosis. In

patients with Sezary Syndrome, malignant T-cells proliferate in the blood, while skin on the surface becomes inflamed, scaly and extremely itchy and doesn't respond to typical skin treatments. The lymphoma circulates in the blood, and tumors spread to the lymph nodes and internal organs. Typically, in the past, as few as 30 percent of patients survived 5 years with Sezary Syndrome; on average, patients survived 40 months after diagnosis.

In the Penn study, patients with advanced Sezary Syndrome received multimodality immunotherapy comprised of extracorporeal photopheresis (ECP) and one or more systemic immunostimulatory agents such as interferon alpha, interferon gamma and/or retinoids.

Patients treated at earlier stages of the disease fared better. A complete response, defined as complete clearance of skin, blood and node involvement for at least 4 weeks, was seen in 30 percent of patients (n= 29). Partial response was found in 45 percent of patients (44). The 5-year survival rate for all groups was 55 percent, and was highest in subsets of patients with stage IIIB disease (80 percent), IVA1 (80 percent), IVA2 (76 percent). Overall median survival time was 65 months; for patients with stage IVA1, median survival was 12 years; stage IVA2, 7 years. For patients with stage IIIB, median survival could not yet be calculated because many patients are still living.

Researchers also identified biological factors to help predict how each patient would respond to treatment. They confirmed that patients with a higher circulating tumor burden had a poor response to treatment. Patients with a higher number of antigen-presenting cells had better outcomes, potentially because antigen-presenting cells process the tumor cells killed by ECP treatment.

Based on this research, the efficacy of combination immunotherapy and increased understanding of the disease response to treatments will

significantly extend the lives of patients with Sezary Syndrome.