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PROSPECTIVE MANAGEMENT OF PRIMARY TESTICULAR LYMPHOMA (PTL) WITH DOXORUBICIN-BASED CHEMOTHERAPY, PROPHYLACTIC INTRATHECAL (IT) METHOTREXATE AND RADIOThERAPY (RT), BUT WITHOUT RITUXIMAB: RESULTS FROM IELSG

Andreas H Sarris, Umberto Vitolo, Emanuele Zucca, George Z Rassidakis, Jeffrey Medeiros, Maria Giuseppina Cabras, Alice Di Rocco, Barbara Pro, Mary K Gospodarowicz and Franco Cavalli on behalf of International Extranodal Lymphoma Study Group (IELSG)

Introduction PTL is a rare extranodal lymphoma characterized by a continuous pattern of systemic relapses in spite of doxorubicin-based therapy. There are also frequent relapses in the contralateral testis and the central nervous system (CNS). Therefore we decided to determine whether prophylaxis of the CNS and the contralateral testis would modify the pattern of relapse of PTL.

Patients and methods From 1993 to February 2002 in IELSG member institutions patients with PTL (presenting with testicular enlargement) were managed with doxorubicin-based therapy according to institutional policy, with the addition of four doses of IT methotrexate (15 mg) during the first 6 weeks. At the end of chemotherapy scrotal RT (30 Gy) was given to all patients and 30-36 Gy nodal RT to those with stage II disease. Rituximab was not used in this cohort because it was not yet generally available for patients with diffuse large B-cell lymphoma.

Results There were twenty seven patients; two refused chemotherapy and/or RT/IT therapy and one RT, leaving 24 eligible for analysis. Median age was 60 years (range 31-80). Ann Arbor stage was I in 17, II in four, and four in three patients. B-symptoms were present in one patient. The right testis was involved in 13 and the left in 11 patients. Serum LDH was elevated in four of 21 with available values. No patient had CNS involvement at diagnosis. Pathology was diffuse large B-cell lymphoma in all patients. Treatment was CHOP in 21, alternating triple therapy in two, and hyper-CVAD in one patient. Three patients died during therapy: one from neutropenic sepsis and two from toxicity of systemic methotrexate. The remaining 21 patients achieved a complete remission. With a median follow-up of 57 months (range 8-123) for survivors, seven patients have relapsed, three in the CNS. There were no testicular relapses. Eight patients have died: three from toxicity during induction, three from relapsed lymphoma, one from gastric carcinoma and one from sudden death, both in complete remission. At 5 years the projected progression free survival was 78%, and survival 66%, but both without an apparent plateau. Freedom from progression in the CNS was 84%, with a plateau.

Conclusions Patients with PTL treated prospectively with doxorubicin-based therapy before the availability of rituximab exhibit the continuous pattern of relapse previously reported. Scrotal RT seems eliminate testicular relapses, and prophylactic IT methotrexate seems to reduce, but not eliminated CNS relapses. These need to be confirmed by longer follow-up. The ongoing IELSG-10 should determine whether the addition of rituximab alters the continuous pattern of systemic relapses. Future studies should determine the molecular basis of the continuous relapses and minimize both systemic and CNS relapses.