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SECOND LINE CHEMOTHERAPY IN HIV-RELATED NON-HODGKIN'S LYMPHOMA: EVIDENCE OF ACTIVITY OF A COMBINATION OF VP16, MITOXANTRONE AND PREDNIMUSTINE IN RELAPSED PATIENTS

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Purpose: To evaluate the feasibility and activity of a second line chemotherapy regimen consisting of VP16, mitoxantrone and prednimustine (VMP) in patients with relapsed or resistant HIV related non-Hodgkin's lymphoma (HIV-NHL).

Patients and methods: Twenty-one patients were consecutively treated. Thirteen patients were resistant to primary chemotherapy and eight patients had relapsed after first complete remission (CR). VP16 and prednimustine were both given orally at doses of 80 mg/m^2 daily for 5 days, and mitoxantrone was given i.v. at a dose of 10 mg/m^2 on day 1; cycles were repeated every three weeks.

Results: Nineteen out of 21 patients are evaluable for response. The median number of cycles actually administered was 2 (range 1-5). A CR occurred in 5 out of 19 patients (26%; exact 95% confidence interval: 9% to 51%). Four of these CRs were observed in the 7 evaluable relapsed patients. Out of 45 cycles evaluable for toxicity, severe neutropenia (<500/ml) occurred in 19 (42%) cycles and severe thrombocytopenia (<25.000/ml) in 6 (13%) cycles. One toxic death occurred due to a sepsis during neutropenia. The overall median survival was 2 months (range, <1-13); the median survival time for the 5 patients with CR (13 months, range 6-13) was statistically significant longer (p=0.004) than that observed in patients without CR (2 months, range <1-7).

Conclusion: Although the overall prognosis of patients with resistant and relapsed HIV-NHL is very poor, palliative therapy with VMP can be effective and relatively safe. Prolonged survivals have been observed in some patients who had relapsed after initial chemotherapy. Supported by AIRC '95 grants.

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CLINICO-PATHOLOGIC CORRELATIONS IN 120 PATIENTS (PTS) WITH HIV-RELATED-SYSTEMIC-NON-HODGKIN'S LYMPHOMA (HIV-NHL): A MONOINSTITUTIONAL STUDY.

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HIV-NHL represent an heterogeneous group of diseases, characterised by the presence of distinct molecular-pathological entities, but overall considered associated with a poor outcome. Few extensive studies on clinico-pathological correlations have been conducted. In this study we examined the relationship between pathological and clinical data obtained from a monoistitutional series of 120 pts with HIV-NHL, diagnosed and treated with chemotherapy from September 1987 to July 1995. The most common histologic type was small non-cleaved cell lymphoma (J group) (33%), followed by miscellaneous NHL (M group) (23%), large cell immunoblastic (H group) (19%), large non-cleaved lymphoma (G group) (15%) and by Ki-1+ anaplastic large cell lymphoma (Ki-1 + ALC) (11%). The clinical presentation of the J group was found significantly different compared with that of diffuse large cell lymphoma (DLCL) group (G, H, Ki-1+ ALC), as follows: better immune function (vs H group, p = 0.02), poorer performance status (PS) (vs G group, p = 0.01), higher abnormal serum LDH level (vs G group, p = 0.02), more disseminated disease (vs H group, p = 0.01), higher involvement of peripheral lymphnodes (vs H group, p = 0.02), bone marrow involvment (vs H group, p = 0.001 and vs G group, p = 0.04), and lesser Waldeyer ring involvement (vs H, G, Ki-1 ALC group, p = 0.001, p = 0.03, p = 0.04, respectively). Within the DLCL group the distribution of cases with respect to presenting clinical features showed male predominance, poorer PS and higher degree of immunodeficiency in Ki-1+ ALC than in G group (p = 0.03, p = 0.02, p = 0.05, respectively). As far as the outcome a better survival was found only in G group (median 16.4 mo) than in H group (median 6.6 mo) (p = 0.01). These findings suggest that G NHL should not be included with H in the same category of DLCL (Harris et al, 1994) since H is associated with poor outcome. Supported by ISS and AIRC grants.

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HIV-RELATED CERVICAL CANCER (CA) IN ITALY; A REPORT OF 54 CASES FROM THE ITALIAN COOPERATIVE GROUP ON AIDS AND TUMORS (GICAT).

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The incidence of cervical intraepithelial neoplasias has increased in HIV-infected women, and invasive cervical ca is currently considered an AIDS defining condition. However the natural history of HIV-related cervical ca is still unknown. To better characterize cervical ca in HIV-infected women we evaluated 54 cases, including 35 (65%) carcinoma in situ (Cis) and 19 (35%) invasive ca, collected by the GICAT between January 1986 and June 1995. The median age was 28 years (range 19-38). The majority (70%) of patients (pts) were intravenous drug users and an history of sexual promiscuity and anogenital HPV-disease was reported by 55% and 88% of pts, respectively.

At the diagnosis of cervical ca, 59% of pts had asymptomatic HIV disease or PGL (category A), while 20% had symptomatic HIV disease not diagnostic for AIDS (category B) and 15% had already a diagnosis of AIDS (category C). Overall the mean CD4 cell count was 360 (± 230.8 SD), however the mean CD4 cell count was significantly lower in the Cis group than in the invasive ca group (279 ± 221.7 vs 455 ± 270.4, p = 0.03). All pts had squamous cell neoplasia. Among pts with invasive ca, 63% had stage I according to FIGO, 21% stage II and 16% stage III-IV. Pts with Cis received cone biopsy (85%) and cryotherapy or laser therapy (15%), whereas pts with invasive ca were treated with major surgery (S) (53%), radiotherapy (24%) or combination therapy (S-chemotherapy) (23%). Complete remission (CR) occurred in 97% of Cis pts and in 81% of invasive ca pts (p = 0.09); the recurrence rate was similar in the two groups (13% vs 20%, respectively), as well as the incidence of AIDS-associated infections during follow up (52% vs 57%, respectively). Median survival was 66 mo for Cis pts and 101 mo for invasive ca pts (p = NS). In conclusion, invasive cervical ca is still occurring in at low rate in pts with HIV-infection in Italy, usually with a relatively good immune function. On the other hand there is a higher prevalence of Cis (65%) emphasizing the importance of integrating gynecological care into medical service for HIV-infected women. Supported by ISS grants.

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EPIRUBICIN, BLEOMYCIN, VINBLASTINE AND PREDNISONE (EBVP) CHEMOTHERAPY (CT) IN COMBINATION WITH ANTIRETROVIRAL THERAPY AND PRIMARY USE OF G-CSF FOR PATIENTS (PTS) WITH HODGKIN'S DISEASE AND HIV INFECTION (HD-HIV).

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Objective: The optimal therapeutic approach for pts with HD-HIV is unknown. In an attempt to improve the results that we obtained in a previous prospective study with EBV without G-CSF (Cancer, 73: 437-44, 1994), in January 1993 we started a second trial consisting of CT, concomitant antiretroviral therapy (AZT or DDI), and G-CSF.

Methods: Up to October 1995, 27(23 M / 4 F) consecutive previously untreated pts (median age 33, range 21-49 years) with HD-HIV were enrolled. Median performance status was 1 (range 1-3). At diagnosis of HD, 7 (26%) of pts had AIDS, 3 (11%) ARC, and 17 (63%) were asymptomatic. Eighty-five per cent of pts had B symptoms at HD presentation. Pts received E 70 mg/m2 i.v. on day 1, B 10 mg/m2 i.v. on day 1, V 6 mg/m2 i.v. on day 1 and P 40 mg/m2 p.o. from day 1 to day 5. Courses were repeated every 21 days for six cycles. AZT (250 mg x 2/day) or DDI (200 or 300 mg x 2/day), when AZT was previously used, were given orally from the beginning of CT. G-CSF was given at the dose of 5 mcg/kg/day s.c. from day 6 to day 20 in all cycles.

Results: Clinico-pathologic characteristics of pts and response to therapy are shown in the table:

# pts entered/evaluable	CD4+ at diagnosis median # (range)	Subtype MC & LD	Stage III & IV	Response OR	CR	DFS at 2 yrs
27/21*	187 (6-812)	18 (66%)	22 (82%)	90%	71%	43%

* 6 pts are still on treatment.

Toxicity was moderate with grade 3-4 leukopenia and thrombocytopenia in 7 (33%) and in 2 (10%) pts respectively. Fifteen out of 21 pts received AZT and 2 pts received DDI. Only 6 (28%) pts had opportunistic infections (OI), during or after CT (median follow-up, 14 months). No change of CD4+ cell count was seen, being the median number 171/mm3 (2-529) after the end of combined therapy. Six out of 15 (40%) pts who achieved a CR relapsed. Overall, HD progression alone and in association with OI was the cause of death in 46% and in 15% of pts respectively. The median survival was 14 months with an actuarial survival rate of 33% at 24 months.

Conclusions: The combined treatment was feasible. However, although the CR rate obtained was satisfactory, the number of relapsed pts was high and overall median survival was not different from our previous experience or from literature. Taking in consideration the moderate toxicity, we are currently considering higher doses of CT at shorter intervals with the support of G-CSF. Supported by AIRC '95 and ISS '95.