

AIDS related malignancies

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TREATMENT OF HIV-RELATED NON-HODGKIN'S LYMPHOMA (NHL) WITH CHEMOTHERAPY (CT) AND GRANULOCYTE COLONY STIMULATING FACTOR (G-CSF): PRODUCTION OF TOXICITY AND OF DAYS OF HOSPITALIZATION WITH CONCOMITANT OVERALL REDUCTION OF THE COST.
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 The aim of this study is to compare toxicity and hospitalization of CT with G-CSF versus CT without G-CSF. We have analyzed 37 consecutive patients (pts) treated with intensive CT regimens, 19 pts from July 89 to June 91 without G-CSF and 18 pts from July 91 to September 92 with G-CSF, 3 mg/kg i.v. daily starting 24 hours after CT for 13 days in all cycles. The CT regimens analyzed were the LNH 84 regimen (Cossu et al, CO 1989, 1:1018-26) and the CHOP-like regimen. CT with G-CSF (LNH 84) (Cossu et al, Ann Oncol 1991, 2:231-0) given for 3-6 cycles. The analysis was performed only for the first 3 cycles of CT. The cost of 1 day of hospitalization in our division is about 450 US dollars.
 Results:

	WITHOUT G-CSF	WITH G-CSF	P VALUE
N. PTS	19	18	
MEDIAN AGE (RANGE)	36 (28-59)	32 (18-51)	
MALE/FEMALE	17/2	15/3	
HISTOLOGY (W.F.)			
CLL/CLL	2/4/12/1	3/1/1/5	
STAGE			
I/II/III/IV	3/5/1/10	2/2/7/7	
MEDIAN CD4+ CELL COUNT/mm ³	235	120	N.S.
RESULTS-toxicity			
- Day of Neut WBC mean (from CT start)	10.8 (±2.8)	8.4 (±1.5)	0.006*
- Neut WBC mean (all pts)	17/2	51/1 (±2.99)	0.09
- Neut WBC mean (pts with CD4+ ≥ 200)	41/1 (2/44)	1/2/1	0.009*
- Mean n. of CT cycles/pts	2.7 (±0.7)	2.4 (±0.8)	NS*
- Pts with documented infections	11/8*	8/6	NS*
- Pts with neutropenia	4/6*	2/2*	0.08*
- Cycles at full dose	8/8*	8/6*	NS*
- Mean delay between the CT cycles (days)	9.0 (±6.4)	4.0 (±4.7)	0.01*
RESULTS-response			
- Overall response	88%	78%	0.22*
RESULTS-cost			
- Mean toxicity-related days of hospitalization	18.0 (±13.2)	6.4 (±9.1)	0.003*
- Mean hospitalization + G-CSF cost/cycle	\$ 3232 (±2283)	\$ 2282 (±1345)	NS*

The side effects of G-CSF were uncommon and mild. We have shown that treatment with G-CSF significantly reduced the mean WBC in pts with CD4+ ≥ 200, the mean delay between the CT cycles and the mean toxicity-related days of hospitalization. Therefore, by comparing with what one might expect, the cost of CT + G-CSF vs CT alone did not increase, actually it decreased. In conclusion, G-CSF in addition to CT should be preferred in the treatment of pts with HIV related NHL. *F-test in 1/2; *Mann-Whitney test; *Fisher test chi-square. Supported in part by grants of the AIDS project, ISS '91 and AIRC '91.

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OLIGOCLONAL IMMUNOGLOBULINS: A POSSIBLE INDEX OF B CELL LYMPHOMA IN AIDS

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In early HIV infection, B cell activation is expressed by increased production of oligoimmunoglobulins and by the appearance of oligoclonal immunoglobulin bands. Also an unusually high incidence of monoclonal gammopathies among LAS (lymphadenopathy syndrome) has been reported. The predisposition for lymphoma in high risk groups, is related to this polyclonal activation of B cells. Therefore the sera of 123 asymptomatic homosexually active men, 20 of whom converted to HIV positivity, were examined for immunoglobulins by isoelectrofocusing (IEF) followed by immunofixation technique. Oligoclonal immunoglobulins or bandings were found in 45%. As distribution of the mono- and biconal gammopathies the following pattern was found: IgGK in 3 cases, IgGα and IgFab each in 1 case; monoclonal heavy chain is observed in 3 cases and biconal IgGKα in 1 case.

In association with the appearance of these oligo-immunoglobulins, an abrupt decline in oligoimmunoglobulin IgGFab was consistent with the developing of lymphoma-like constitutional symptoms; 10% developed extra lymphoma. The conclusion of this study is, that in HIV positive individuals demonstration of oligo-immunoglobulins IgG, with abrupt decline of IgGFab, is related to the polyclonal B cell activation.

In addition this may indicate clinical progression and predisposition for B cell lymphoma.

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MALIGNANT DISEASES IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

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We observed 49 malignancies in HIV-positive patients (pts): 35 with Kaposi's sarcoma (KS), 10 with non-Hodgkin lymphoma (NHL), (7 diffuse, 3 primary CNS lymphomas), 1 with Hodgkin's disease (HD) and 3 with epithelial tumors. The KS group was treated with alpha-2b interferon, monochemotherapy (doxorubicin or bleomycin), radiotherapy (RT) or intralesional vinblastine. Median survival (MS) from KS diagnosis was 10 months (m) (6-18). Diffuse NHL group was treated with CHOP, m-BACOD and/or RT. MS from NHL diagnosis was 4 m (2-10). Primary CNS lymphoma group received RT and the MS was 3 m (2-5). HD pt was treated with MOPP/ABV and the survival was 20 m. Pts with epithelial tumors did not received specific treatments for their tumors. MS was 5 m (1-9). The survival in HIV-positive pts with malignancies is very poor and better treatments need to be developed.

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MALIGNANT LYMPHOPROLIFERATIVE DISEASES (MLD) IN PATIENTS SEROPOSITIVE FOR THE HIV:

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40 patients (pts) with MLD in HIV+ pts are analyzed. Median age 32 years (range 15-42). 22 pts (60%) intravenous drug abuse (IVDA), 12 homosexual (30%), 6 (7.5%) other factors. 11 pts (27.5%) previous AIDS diagnoses, 17 (50%) < than 200 CD4/uL. 26 were systemic non-Hodgkin lymphoma (NHL) of high and intermediate grade, including 14 small non-cleaved, 6 immunoblastic or large cell, 2 plasmablastic and 4 high grade not otherwise specified. Six pts primary central nervous system (CNS) lymphoma (PCL). Eight Hodgkin's disease. 35 were treated and 33 are evaluable for response (2 too early to evaluate). Five pts diagnosed postmortem. 13 (40%) Complete Response (CR), 8 (24%) Partial Response (PR) and 12 (36%) treatment failures. With a median follow-up of 10 months, 11 out of 21 (52%) with objective response (CR + PR) relapsed (6 leptomeningeal, 5 local). 30 pts have died: 25 disease-related, 2 toxic deaths during treatment, 3 from opportunistic infections. 2 pts were lost to follow-up. 8 pts are alive and well, at median follow-up of 10.5 months (range 3-85 months). Median survival for the whole group was 5 months (Kaplan-Meier). Pts with PCL (p<0.01), Karmofsky performance status (KPS) less than 70% (p<0.01) and previous criteria for AIDS (p<0.02) had a significant shorter survival (Mantel-Haenszel). Conclusion: The existence of long survivors, specially in patients without antecedents AIDS criteria, KPS > 70% and without PCL, encourages to treat these pts and search for effective treatments for both the MLD and the underlying HIV infection.

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EPIDEMIC KAPOSI'S SARCOMA: EXPERIENCE AT THE JOHANNESBURG HOSPITAL (1977-1990).

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The most frequent of the AIDS-related neoplastic diseases is Kaposi's Sarcoma (KS).

During 1977-1990, 47 HIV positive patients (pts) were referred to our department. 46 were male patients. 33 (70%) pts were black and 14 (30%) pts white. 28 (60%) had multiple skin lesions.

Stage of disease: 14 (30%) early disease (confined to the skin only) 33 (70%) - advanced disease (disseminated skin involvement, visceral organs and/or lymph nodes). Treatment modalities included various chemo and radiotherapeutic regimens.

Response: 16 (34%) pts - partial remission or stable disease; 20 (43%) - disease progression. 11 pts were lost to follow-up but had an active unresponsive disease when last seen.

Statistical analysis

Compared to 61 HIV-ve KS patients, the HIV status was most strongly associated with progression of diseases. Given the HIV status, other variables (systemic signs, opportunistic infections, stage of disease, sites of lesions) were no longer statistically significantly associated with progression of disease.

Conclusions: The HIV status is the only variable to independently predict progression of disease on therapy.

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AIDS ASSOCIATED NON HODGKIN LYMPHOMAS (NHL): RETROSPECTIVE ANALYSIS

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Between 2/83 and 12/92, 550 AIDS patients according CDC classification were assisted at Huesped Foundation and/or Fernandez Hospital, 19/550 (3.4%) developed AIDS related NHL. 17 high grade, 2 intermediate grade. Homosexuals 8, IVDA 10, heterosexual 1. Age: 29.5 (r 17-66). P.S. (ECOG): 2:9, 3:6, 4:4. Stage: I: 1, II:3, III:5, IV: 10. Localizations: Nodes: 18; Gastrointestinal (G.I.): 10; Bone Marrow: 5; Lung: 4; CNS: 3 - Bulky Disease: 7. Treated: 16. Surgery: 1. Radiotherapy: 3. Chemotherapy: 16; anthracyclin regimen: 9, Oral etoposide: 7. Results:

	NHL GROUP	CHOP ± BLEO	VP 16	P
RR	12/16 (CR:6; PR:6)	8/9 (CR:5; PR:3)	4/7 (CR:1; PR:3)	NS
TTP	5.4m (r3-15+m)	5.6m (r3-15+m)	5.2m (r3-10+m)	NS
OS	6.3m (r1-17+m)	8.3m (r4-17+m)	5.3m (r1-12+m)	NS
A/D	6/16	3/9	3/7	NS

RP: Response Rate - TTP: Time to progression - OS: overall survival - A/D: alive/death - 13/19 pts are dead. Infection 7/13 drug related death: 2/13, tumor progression: 4/13. Conclusions: 1) Aggressive NHL represents 3.4% of AIDS pts; 2) We couldn't find any difference in RR, TTP and OS between both chemotherapy regimens; 3) G.I. involvement was a frequent extranodal site; 4) Infection was the main cause of death.