# Stanford V regimen and concomitant HAART in 59 patients with Hodgkin disease and HIV infection

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A phase 2 prospective study was performed to evaluate the feasibility and activity of a short, dose-intensive chemotherapy regimen and radiotherapy (the Stanford V regimen) plus highly active antiretroviral therapy (HAART) and granulocyte colony-stimulating factor (G-CSF) support in patients with Hodgkin disease and HIV infection. Fifty-nine patients were enrolled. Stanford V was well tolerated and 69% of the patients completed treatment with no dose reduction or delayed chemotherapy administration. The most important dose-limiting side effects were bone marrow toxicity and neurotoxicity. Complete remission was achieved by 81% of the patients, and after a median follow-up of 17 months 33 patients (56%) were alive and disease-free. The estimated 3-year overall survival (OS), disease-free survival (DFS), and freedom from progression (FFP) were 51%, 68%, and 60%, respectively. Probability of FFP was significantly ($P$ = .02) higher among patients with an International Prognostic Score (IPS) of 2 or lower than in those with an IPS higher than 2, and the percentages of FFP at 2 years in these groups were 83% and 41%, respectively. Similarly, the probability of OS was significantly ($P$ = .0004) different in the 2 groups, and the percentages of OS at 3 years were 76% and 33%, respectively. Our data confirm that the Stanford V regimen with concomitant HAART is feasible and active in an HIV setting. However, a more intensive approach should be considered in patients with high IPSs. (Blood. 2002; 100:1984-1988)

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## Introduction

Hodgkin disease (HD) is the most common non–AIDS-defining tumor occurring in patients with HIV infection.[1-3] All assessable data document an usually aggressive behavior of HD in patients with HIV (HD-HIV) as compared with HD outside the HIV setting, including higher frequency of unfavorable histological subtypes such as mixed cellularity and lymphocyte depletion, advanced stage at presentation, and poor treatment outcome. Bone marrow involvement has been described in 40% to 50% of HD-HIV patients, in addition to unusual sites of extranodal involvement.[4-6]

The optimal therapeutic approach for these patients is still unknown because of the lack of experience with this setting; however, it is clear that chemotherapy and/or radiotherapy with an intent to cure should be assessed in all patients with HD-HIV. Only 3 phase 2 prospective studies have been published, showing a short median overall survival (OS) ranging from 11 to 18 months, despite a relatively good overall response rate (62%-91%). The cause for such an unfavorable outcome may be both the underlying HIV infection and the short disease-free survival (DFS), which, in turn, may be due to the fact that antineoplastic therapy is less effective in HD-HIV patients than in the general population.[7-9]

Both of our first 2 prospective studies were carried out before highly active antiretroviral therapy (HAART) was introduced into clinical practice. In 1989, when toxicity of chemotherapy and prednisone in the HIV setting was a main concern, we treated 17 patients with HD-HIV using the relatively low-toxicity epirubicin, bleomycin, and vinblastine (EBV) regimen in combination with zidovudine, the only effective anti-HIV drug available at that time. This approach yielded a 53% complete remission (CR) rate with a median OS of 11 months and a 55% 2-year DFS rate.[7] Then in 1993, in an attempt to improve these findings, we conducted another prospective study on the combination of the epirubicin, vinblastine, bleomycin, and prednisone (EBVP) regimen with the primary use of granulocyte colony-stimulating factor (G-CSF), which had just been introduced into clinical practice. The results of this trial on 35 patients were better and showed a CR rate of 74% with 3-year OS and DFS rates of 32% and 53%, respectively.[8]

Later on, when the HAART era had already begun, the results of a study on 21 patients treated with the gold-standard doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) regimen were reported in the United States by the AIDS Clinical Trial Group (ACTG). The CR rate was 43%, with an overall objective response rate of 62%. Median survival was 18 months and DFS 13 months.[9]

In 1997 we took advantage of the availability of both HAART and G-CSF in clinical practice, as well as our improved experience in the management of patients with lymphomas and HIV infection, and designed a new approach for patients with HD-HIV. Their

outcome was still unfavorable, mainly because their CR and DFS rates were lower than those in the general population; hence, we figured that an aggressive regimen such as Stanford V, the short-term (12 weeks) intensive chemotherapy regimen with adjuvant radiotherapy developed at Stanford University for unfavorable HD in the general population,[10] would be the ideal test in this group with a view to improving their poor outcome. At the same time, however, we wondered about the feasibility of such an approach, which required a high-intensity chemotherapy regimen and the concomitant use of HAART. The results of a phase 2 study with Stanford V in combination with HAART and G-CSF support in patients with HD-HIV are reported here.

## Patients and methods

### Inclusion criteria

In order to be enrolled patients had to meet the following inclusion criteria: biopsy-proven HD; age older than 18 years; confirmed HIV infection; clinical or pathologic stage II, III, IV according to Ann Arbor staging or stage I with adverse prognostic factors, defined as the presence of bulky disease (tumor mass > 5 cm) and/or B symptoms; no previous chemotherapy for HD; World Health Organization (WHO) performance status (PS) of 3 or lower; no concomitant or previous malignancy except for nonmelanoma skin cancer or in situ cervical carcinoma; total bilirubin level lower than 1.5 mg/dL; creatinine level lower than 2.0 mg/dL; granulocyte count higher than 1000 cells/dL; platelet count higher than 100 000 cells/dL (unless the last 2 findings were caused by bone marrow involvement); the study was approved by the review board at the Aviano Cancer Center and all patients signed an informed consent according to the Declaration of Helsinki.

### Staging

All patients were evaluated for history and underwent a physical examination, including height, weight, and WHO performance status; measurement of all involved palpable lesions; complete blood cell count; blood chemistry; chest radiography; computer tomography of the thorax and abdomen; bone marrow aspiration and biopsy; electrocardiogram and left ventricular ejection fraction evaluation; CD4 cell count; and HIV viral load. The Ann Arbor staging system was applied.[11]

### Treatment

The Stanford V chemotherapy regimen was administered over 12 weeks. The drugs and doses given intravenously each week were as follows: doxorubicin (25 mg/m$^2$) in weeks 1, 3, 5, 7, 9, and 11; vinblastine (6 mg/m$^2$) in weeks 1, 3, 5, 7, 9, and 11; mecloretamine (6 mg/m$^2$) in weeks 1, 5, and 9; etoposide (60 mg/m$^2$) for 2 successive days in weeks 3, 7, and 11; vincristine (1.4 mg/m$^2$; maximum dose 2 mg) in weeks 2, 4, 6, 8, 10, and 12; and bleomycin (5 U/m$^2$) in weeks 2, 4, 6, 8, 10, and 12. Prednisone (40 mg/m$^2$) was given orally every other day for 10 weeks and tapered by 10 mg every other day between weeks 10 and 12. During the whole 12-week chemotherapy cycle, patients received double-strength trimethoprim/sulfametoxazole by mouth once a day and 100 mg fluconazole by mouth every day.

G-CSF was used prophylactically at a dose of 5 μg/kg/d from day 3 to day 13 (with a pause on day 8) and from day 17 to 26 (with a pause on day 22), whereas the schedule was unchanged in the subsequent cycles.

HAART was given concomitantly from the beginning of chemotherapy, regardless of CD4 cell count and HIV viral load. HAART was selected on the basis of the patient's prior antiretroviral exposure.

If the granulocyte count was lower than 500/dL on the day of treatment, therapy was postponed to the following week, whereas if it remained between 500 and 1000/dL, the doses of mecloretamine, doxorubicin, vinblastine, and etoposide were reduced to 75% of the full doses. The vincristine and bleomycin doses were delivered regardless of the granulocyte cell count and were decreased only if there were other reasons for doing so.

Eligibility for involved field radiotherapy was possible for all patients who had achieved partial remission (PR) and those who were in CR and showed initial bulky mediastinal disease and/or initial, single, or confluent nodal masses 5 cm or larger in diameter. The total dose for initial bulky HD was 36 Gy delivered in 2-Gy fractions 5 days per week.

### Evaluation of antitumor response

CR was defined as the complete absence of clinically detectable tumors and normalization of previously abnormal radiographic findings persisting for at least 4 weeks. PR was defined as a reduction of at least 50% in the product of the perpendicular diameters of all tumors assessed by physical examination or radiographic checkup persisting for more than one month with no new lesions occurring. Stable disease (SD) was described as a change of less than 25% in the product of the perpendicular diameters of all tumors. Progressive disease (PD) was defined as an increase of more than 25% in the measured lesions or the occurrence of new lesions.

### Evaluation of toxicity

Toxicity was rated according to WHO criteria.[12]

### Statistical methods

Survival was calculated from the date chemotherapy was started to death from any cause or to the last time the patient showed up. DFS was calculated for patients with CR from the first CR recorded until relapse or until the last known date on which the patient was disease-free. Freedom from progression (FFP) was determined from the beginning of treatment to disease progression, relapse, or last follow-up. OS, DFS, and FFP were evaluated according to the Kaplan-Meier method[13] and differences between subgroups were assessed by means of the log-rank test.[14] Multivariate analysis of survival was performed with the Cox proportional hazards model (HR) and 95% confidence interval (CI),[15] including all variables that were significantly associated with prognosis in the univariate analysis. Differences between qualitative parameters were performed by $\chi^2$ test.[16] In all cases, statistical significance was claimed for $P$ of .05 or lower (2 sides).

## Results

From May 1997 to October 2001, 59 consecutive patients with HD-HIV were treated in the framework of this prospective phase 2 study within the European Intergroup Study HD-HIV and all of them are evaluable for response, toxicity, and survival. Of this cohort, 16 patients were treated at the Aviano Cancer Center in Italy, 10 at the Pitié Salpetrière in Paris, France, and the remaining 33 at 15 Italian centers. The patients' pretreatment characteristics and HD features are listed in Table 1. Fifty-one (86%) of the 59 patients were male and 8 (14%) were female. Median age was 38 years (range, 28-64 years). WHO PS was 0 or 1 in 42 patients (71%) and 2 or 3 in the remaining 17 (29%). Disease staging, according to the Ann Arbor system, was as follows: stage I, 4 patients (7%); stage II, 13 patients (22%); stage III, 15 patients (25%); stage IV, 27 patients (46%). Six patients (10%) had bulky disease, whereas 44 (75%) had constitutional B symptoms. Twenty-eight patients (31%) showed extranodal involvement. Bone marrow was involved in 24 patients (41%), spleen in 23 (39%), liver in 10 (17%), lung in 1 (2%), rectum in 1 (2%), and adrenal gland in 1 (2%). As for the histological subtype of HD, mixed cellularity was determined in 27 cases (46%), nodular sclerosis in 18 (30%), and lymphocyte depletion in 4 (7%). In 10 cases (17%), the histological subtype could not be classified.

The patients' International Prognostic Scores (IPSs)[17] were as follows: 2 patients (3%) had an IPS of 0; 10 (17%) had an IPS of 1;

**Table 1. Characteristics of patients (n = 59) with Hodgkin disease and HIV infection**

| Patient characteristics | No. | % |
|---|---|---|
| Sex | | |
| Male | 51 | 86 |
| Female | 8 | 14 |
| WHO PS | | |
| 0 to 1 | 42 | 71 |
| 2 to 3 | 17 | 29 |
| Stage | | |
| I to II | 17 | 29 |
| III to IV | 42 | 71 |
| Bulky disease | 6 | 10 |
| B symptoms | 44 | 75 |
| Sites involved | | |
| Lymph nodes only | 31 | 53 |
| Bone marrow | 24 | 41 |
| Spleen | 23 | 39 |
| Liver | 10 | 17 |
| Lung | 1 | 2 |
| Rectum | 1 | 2 |
| Adrenal gland | 1 | 2 |
| Histology | | |
| Mixed cellularity | 27 | 46 |
| Nodular sclerosis | 18 | 30 |
| Lymphocyte depletion | 4 | 7 |
| Not classifiable | 10 | 17 |

The median age of the patients was 38 years (range, 28-64 years).

14 (24%) had an IPS of 2; 14 (24%) had an IPS of 3; 7 (12%) had an IPS of 4; 10 (17%) had an IPS of 5; and 2 (3%) had an IPS of 6. In particular, 51 patients (86%) were male, 15 (25%) were aged 45 years or older, 27 (46%) had stage IV disease, 33 (56%) had an albumin level below 4 g/dL, 30 (51%) had a hemoglobin level below 10.5 g/dL, 1 (2%) had a white cell count of 15 000/dL or higher, and in 17 cases (29%) the lymphocyte count was lower than 600/dL or lower than 8% of the white cell count. Therefore, 26 patients (44%) had an IPS of 2 or lower, and 33 (56%) had an IPS higher than 2 (Table 2).

Pretreatment immunological characteristics and HIV status are shown in Table 3. In line with the epidemiology of HIV infection in Italy, 29 of our patients (48%) were intravenous drug users. Seventeen (29%) were male homosexuals, and 13 (23%) reported heterosexual relationships as their only risk factor for HIV infection. Twelve (20%) of the 59 patients had been diagnosed with AIDS before being diagnosed with HD (*Pneumocystis carinii* pneumonia [PCP] in 5 cases, esophageal candidiasis in 4 cases, disseminated tuberculosis in 2 patients, and cerebral toxoplasmosis in 1). The median CD4 cell count was 238/dL (range, 32-1008/dL); 34 (58%) of the patients had a detectable HIV viral load, with a

**Table 2. International Prognostic Scores[17] of patients with Hodgkin disease and HIV infection**

| Score | No. | % |
|---|---|---|
| 0 | 2 | 3 |
| 1 | 10 | 17 |
| 2 | 14 | 24 |
| 3 | 14 | 24 |
| 4 | 7 | 12 |
| 5 | 10 | 17 |
| 6 | 2 | 3 |
| 7 | 0 | — |

**Table 3. Pretreatment HIV-related characteristics of patients with Hodgkin disease and HIV infection**

| Patient characteristics | No. | % |
|---|---|---|
| Risk factor | | |
| Intravenous drug use | 29 | 48 |
| Homosexual relations | 17 | 29 |
| Heterosexual relations | 13 | 23 |
| AIDS diagnoses before HD diagnosis | 12 | 20 |
| *Pneumocystis carinii* pneumonia | 5 | 42 |
| Esophageal candidiasis | 4 | 33 |
| Disseminated tuberculosis | 2 | 17 |
| Cerebral toxoplasmosis | 1 | 8 |
| HIV viral load | | |
| Undetectable | 25 | 42 |
| Detectable | 34 | 58 |

The median CD4 cell count per deciliter was 238 (range, 32-1 008 cell count/dL); the median HIV viral load (copies per deciliter) was 3400 (range, 60-455 000 copies/dL).

median value of 3400 copies/dL (range, 60-455 000 copies/dL); and 36 (61%) had received HAART for more than 3 months at the onset of HD.

Of the 59 patients, 52 (88%) were given HAART concomitantly with the Stanford V regimen. Seven patients were not given antiretroviral treatment, as a result of their physicians' decisions in 5 cases and because of the patient's desire in 2 cases.

The Stanford V regimen was well tolerated, and 41 patients (69%) completed the treatment plan without any dose reduction or delay in chemotherapy administration. Toxicity made it necessary for 18 patients (31%) to reduce the dosage of all drugs but prednisone to 75% or less of the amount they should have been given. The most important dose-limiting side effect was bone marrow toxicity. Actually, despite the use of G-CSF, 46 patients (78%) developed grade 3 or 4 neutropenia (9 and 37 cases, respectively). Grade 3 or 4 anemia was observed in 28 patients (47%) (grade 3 in 20 cases and grade 4 in 8 cases), whereas 13 patients (22%) had grade 3 or 4 thrombocytopenia (2 and 11 cases, respectively). Sixteen patients (27%) had fever during neutropenia, with 5 (8%) cases of documented sepsis. One patient died of septic shock. Four major AIDS-defining events were observed during chemotherapy or within one month after chemotherapy was concluded: tuberculosis in 2 patients, PCP in 1 patient, and wasting syndrome in 1 patient. Moreover, 32 patients (54%) developed neurotoxicity, including grade 2 or 3 constipation (2 and 5 patients, respectively), grade 1 neuromuscular toxicity (4 patients), and grade 2 or 3 neurosensory toxicity (9 and 12 patients, respectively). One patient (2%) suffered from grade 2 hepatic toxicity. No difference in the administration of the Stanford V regimen or in toxic effects was found between patients with IPSs of 2 or lower and those with IPSs of more than 2.

We observed also that the underlying HIV infection did not worsen at the end of chemotherapy. Actually, 3 months after the end of the Stanford V regimen the median CD4 cell count was 200/dL (vs 238/dL when HD was diagnosed), and only 4 patients (16%) with undetectable HIV viral load before chemotherapy had become positive as a result of HIV progression. On the contrary, 16 (47%) of 34 patients with a detectable viral load at the beginning of treatment with the Stanford V regimen had become negative following the concomitant HAART administration.

Of 10 eligible patients, only 6 received radiotherapy. Two patients refused treatment, one because of drug addiction and the other on advice
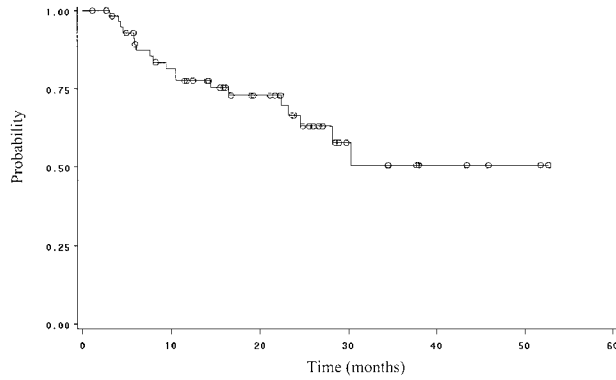
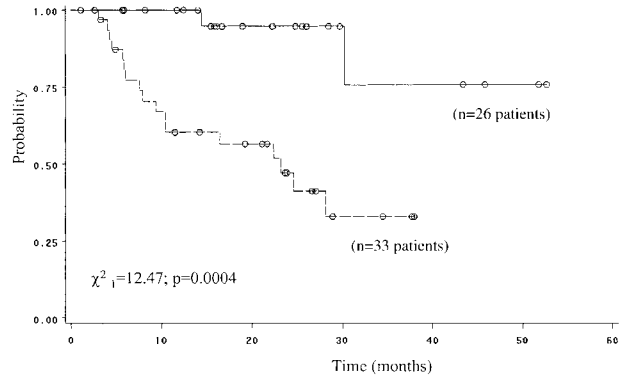**Figure 1. Overall survival of 59 patients with HD-HIV.**



**Figure 3. Survival of 59 patients with HD-HIV, by IPS ($\leq$ 2 vs > 2).**

of a physician. All patients but one, who had developed tuberculosis, completed the radiotherapy cycle as planned.

Overall, 53 (89%) of the 59 patients had an objective response: 48 (81%) achieved CR and 5 (8%) achieved PR. Six patients (10%) progressed. The CR rate varied significantly as a function of IPS: 26 (100%) of 26 patients with IPSs of 2 or less achieved CR, versus 22 (67%) of 33 patients with IPSs of more than 2 ($P = .001$).

After a median follow-up of 17 months, 33 (56%) of the patients were alive and disease-free. The estimated 3-year OS, DFS, and FFP rates are 51% (Figure 1), 68%, and 60% (Figure 2), respectively. Nineteen patients (32%) had died: 13 from HD progression, 2 following opportunistic infections, 1 from a treatment-related complication, and 3 of different causes (2 of liver cirrhosis and 1, who had primary pulmonary hypertension, from myocardial infarction).

In the univariate analysis, the patient's risk factor for HIV infection, the presence of B symptoms, and an IPS higher than 2 were associated with a shorter survival. However, in the multivariate analysis an IPS higher than 2 was the only parameter associated with a significantly shorter survival (HR = 5.8; 95% CI, 1.0-33.4; $P = .05$). In fact, the median OS was significantly shorter in patients with IPSs higher than 2 than in those whose scores were 2 or lower (23 months vs not reached). The probability of OS was significantly ($P = .001$) higher among patients with an IPS of 2 or lower than in those with scores higher than 2, and the percentages of OS at 3 years in the 2 groups were 76% and 33%, respectively (Figure 3). Similarly, probability of FFP was significantly different in the 2 groups ($P = .02$), and the percentages of FFP at 3 years were 83% and 41%, respectively (Figure 4).
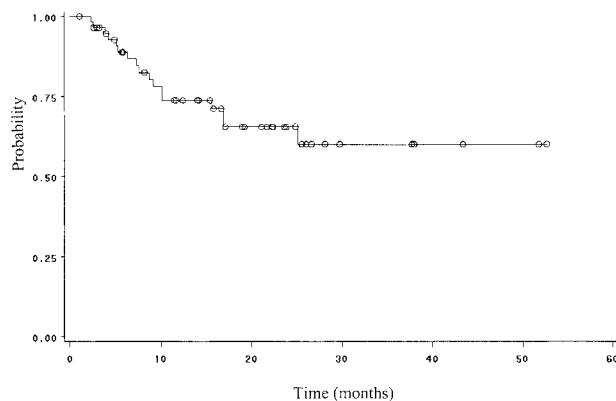
## Discussion

This is the largest prospective study ever performed in patients with HD-HIV treated with concomitant aggressive chemotherapy and HAART. The baseline characteristics of our patients are similar to those reported by previous prospective studies, both for HD characteristics (ie, histological subtypes, advanced stage, B symptoms, and extranodal involvement) and for HIV infection (ie, median CD4 cell count, previous diagnosis of AIDS).

The results of our study show that an approach combining aggressive chemotherapy and HAART is feasible; we report only one treatment-related toxic death. Myelosuppression and neurotoxicity are the most important dose-limiting side effects. Indeed, the incidences of grade 3 or 4 neutropenia, anemia, and thrombocytopenia were 78%, 47%, and 22%, respectively, whereas 29% of our patients experienced grade 3 neurotoxicity.

The high incidence of bone marrow suppression in the present study can be related to the dose intensity of the Stanford V regimen and to the concomitant use of HAART, which included myelotoxic drugs. Eleven (21%) of 52 patients who received HAART concomitantly with Stanford V took zidovudine, and 35 (67%) took lamivudine. Similarly, the high incidence of neurotoxicity can be ascribed to the fact that the HAART regimen included a neurotoxic drug (didanosine, zalcitabine, or stavudine) for 43 (83%) of the 52 patients.

A comparison of toxicity between our study and the ACTG study using the classic ABVD shows a similar incidence of thrombocytopenia (22% in our series vs 24% in the ACTG group), whereas the incidence of neutropenia and anemia was higher in our study (78% vs 52% and 47% vs 24%, respectively).
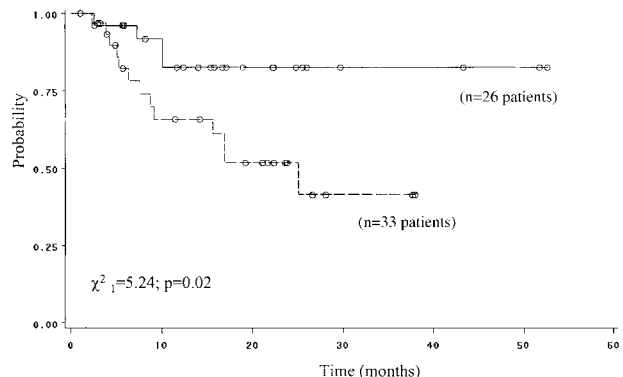


**Figure 2. Overall freedom from progression of 59 patients with HD-HIV.**



**Figure 4. Freedom from progression of 59 patients with HD-HIV, by IPS ($\leq$ 2 vs > 2).**

Moreover, the incidence of opportunistic infections (OIs) during chemotherapy or within 3 months of completion of chemotherapy was significantly lower in our study (7%) than in the ACTG study (29%). This can be explained only partly by the higher median CD4 cell count of our patients (238/dL) compared with that of the patients treated with ABVD (113/dL); we feel the concomitant use of HAART and chemotherapy is the most important factor for the decrease in OIs. Interestingly, the incidence of neutropenia in our study is similar to the rate reported by Horning et al,[10] who administered Stanford V in the general population, even though anemia and thrombocytopenia are recorded more often in the HIV setting, which may be due to the use of HAART and to HIV-related myelodysplasia. We also observed grade 3 neurotoxicity in 29% of our patients, which is similar to the rate reported with Stanford V in the general population (35%).

A comparison of the present study with the other prospective studies in the HIV setting published so far shows that CR, DFS, and OS rates were significantly improved in the present study. CR was achieved by 81% of our patients, versus 74% in our previous EBVP study and 43% in the ABVD study. Median OS was 16 and 18 months, respectively, for patients treated with EVBP and ABVD, whereas it has not yet been reached in the present study, with an estimated 3-year OS of 51%. Moreover, the 3-year DFS of the present study is significantly better than that observed with EBVP (53%) and ABVD (median duration 13 months). Whether or not the better survival rate is related to a decrease in the number of AIDS-related deaths after the introduction of HAART in the management of HIV patients, it seems clear that the longer DFS is related to the more effective chemotherapy employed. However, we think that, as we saw in our study patients with HIV-related non-Hodgkin lymphoma, the use of HAART during and after chemotherapy could prolong the duration of CR.[18]

In the general population, the use of the Stanford V regimen has been associated with a 5-year FFP and OS of 89% and 96%, respectively.[10] As expected, the outcome of our patients was worse than that of patients without underlying HIV infection: with a median follow-up of 17 months, we reported 3-year FFP and OS rates of 51% and 60%, respectively.

Furthermore, the outcome of our patients was influenced significantly by their IPSs at diagnosis, which was the only parameter affecting the survival rate in the multivariate analysis: OS was significantly shorter in the patients with higher IPSs (> 2) than in those with lower IPSs (≤ 2), and the OS rate at 3 years was higher in the lower-IPS group (76%) than in the higher-IPS group (33%). Similarly, the 3-year FFP rate was significantly better in the former group than in the latter group (83% vs 41%). These findings are in accordance with those reached for the patients with HD in the general population treated with Stanford V, with both OS and FFP being significantly better in patients with IPSs of 2 or lower.[10]

In conclusion, our data show that the Stanford V regimen with concomitant HAART is feasible and highly active in this setting and HIV infection is not a limiting factor for its use. Moreover, the concomitant use of HAART does not seem to increase the toxicity of the Stanford V regimen; rather, it seems to significantly reduce the occurrence of OIs during treatment and follow-up.

However, the outcome is worse for patients with IPSs of 2 or higher, with HD representing the leading cause of death. Hence, in view of the better control of HIV infection and the more effective management and prophylaxis of OI that HAART allows, and also the feasibility of aggressive regimens in this setting, our opinion is that a more aggressive approach should be strongly considered in patients with adverse prognostic factors.

## References

1. Franceschi S, Dal Maso L, Arniani S, et al. for the Cancer and AIDS Registry Linkage Study. Risk of cancer other than Kaposi's sarcoma and non-Hodgkin's lymphoma in persons with AIDS in Italy. Br J Cancer. 1998;78:966-970.
2. Lyter DW, Bryant J, Thackeray R, et al. Incidence of human immunodeficiency virus-related malignancies in a large cohort of homosexual men. J Clin Oncol. 1955;13:2540-2546.
3. Serraino D, Pezzotti P, Dorrucci M, et al. for the HIV Italian Seroconversion Study Group. Cancer incidence in a cohort of human immunodeficiency virus seroconverters. Cancer. 1997;79:1004-1008.
4. Tirelli U, Errante D, Dolcetti R, et al. Hodgkin's disease and human immunodeficiency virus infection: clinicopathologic and virologic features of 114 patients from the Italian Cooperative Group on AIDS and Tumors. J Clin Oncol. 1995;13:1758-1767.
5. Spina M, Vaccher E, Nasti G, et al. Human immunodeficiency virus-associated Hodgkin's disease. Semin Oncol. 2000;27:480-488.
6. Andrieu JM, Roithmann S, Tourani JM, et al. Hodgkin's disease during HIV-1 infection: the French registry experience. Ann Oncol. 1993;4:635-641.
7. Errante D, Tirelli U, Gastaldi R, et al. Combined antineoplastic and antiretroviral therapy for patients with Hodgkin's disease and human immunodeficiency virus infection. A prospective study of 17 patients. Cancer. 1994;73:437-444.
8. Errante D, Gabarre J, Ridolfo AL, et al. Hodgkin's disease in 35 patients with HIV infection: an experience with epirubicin, bleomycin, vinblastine and prednisone chemotherapy in combination with antiretroviral therapy and the primary use of G-CSF. Ann Oncol. 1999;10:189-195.
9. Levine AM, Li P, Cheung T, et al. Chemotherapy consisting of doxorubicin, bleomycin, vinblastine and dacarbazine with granulocyte-colony-stimulating factor in HIV-infected patients with newly diagnosed Hodgkin's disease: a prospective, multi-institutional AIDS Clinical Trials Group Study (ACTG 149). J Acquir Immune Defic Syndr. 2000;24:444-450.
10. Horning SJ, Hoppe RT, Breslin S, et al. Stanford V and radiotherapy for locally extensive and advanced Hodgkin's disease: mature results of a prospective clinical trial. J Clin Oncol. 2002;20:630-637.
11. Carbone PP, Kaplan HS, Musshoff K, Smithers DW, Tubiana M. Report of the Committee on Hodgkin's Disease Staging Classification. Cancer Res. 1971;31:1860-1861.
12. Miller AB, Hoogstragen B, Staquet M, Winkler A. Reporting results of cancer treatment. Cancer. 1981;47:207-214.
13. Kaplan EL, Meier P. Non-parametric estimation of incomplete observations. J Am Stat Assoc. 1958;53:270-283.
14. Mantel N. Evaluation of survival data and two new rank order statistics arising in its consideration. Cancer Chemother Rep. 1966;50:163-170.
15. Cox DR. Regression models and life tables. J R Stat Soc B. 1972;34:187-220.
16. Armitage P, Berry G. Statistical Methods in Medical Research. 2nd ed. Oxford, England: Blackwell Scientific Publications; 1987.
17. Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease. N Engl J Med. 1998;339:1506-1514.
18. Vaccher E, di Gennaro G, Schioppa O, et al. Highly active antiretroviral therapy (HAART) significantly improves disease free survival (DFS) in patients (pts) with HIV-related non-Hodgkin's Lymphoma (HIV-NHL) treated with chemotherapy (CT). Proceedings of ASCO. 2001;1122:281a.