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Malignant Lymphomas

Efficacy of a modified Stanford V regimen in patients with advanced Hodgkin's lymphoma

We report treatment results obtained with a modified Stanford V regimen in 32 patients with advanced Hodgkin's lymphoma (stage II bulky disease, III, IV). Treatment results were not superior to those achieved with conventional treatment (ABVD) in terms of complete remission and survival rates (progression-free survival and overall survival at 3 years: 66% and 91%, respectively).

haematologica 2004; 88:751-752
(*http://www.haematologica.org/journal/2004/6/751*)

Cure rates for patients with advanced Hodgkin's lymphoma range between 60 and 70% when treated with conventional chemotherapy regimens. The combination of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) emerged as the standard therapy because of its low toxicity profile and equivalent efficacy when compared to other regimens.[1] The Stanford V program is an abbreviated intensified chemotherapy regimen which has been proposed as a favorable alternative, with 5-year freedom-from-progression rates reported to be between 85% and 89% and an overall survival (OS) of 96%.[2-4]

We treated 32 patients with previously untreated, histologically proven, locally extended or advanced (stage II with bulky disease of more than 5 cm, stage III or IV disease) Hodgkin's lymphoma with a modified Stanford V regimen, in which mechlorethamine was replaced by cyclophosphamide because of the latter's lower leukemogenic risk. Chemotherapy was given weekly for 12 weeks as follows: vinblastine 6 mg/m^2 and doxorubicin 25 mg/m^2 in weeks 1, 3, 5, 7, 9 and 11; vincristine 1.4 mg/m^2 (maximum dose 2 mg) and bleomycin 5 U/m^2 in weeks 2, 4, 6, 8, 10, and 12; cyclophosphamide 650 mg/m^2 in weeks 1, 5, and 9; and etoposide 120 mg/m^2 on weeks 3, 7, and 11; prednisone 40 mg/m^2 every other day from week 1 until week 10, and tapered during weeks 11 and 12. Local radiotherapy with 36 Gy was scheduled for patients with initial bulky disease > 5 cm or sites of partial remission. As a control group we selected a historical group of 64 patients matched for age, sex, histotype, stage and presence of bulky disease who had been treated with standard ABVD administered every 28 days. Patients received a mean of 7.2±1.6 cycles. The patients' characteristics are listed in Table 1.

Therapy according to the modified Stanford V regimen was well tolerated, without major toxicities or dose reductions: dose intensity was 0.93±0.098 (mean±standard deviation) of the planned dose. At a median follow-up of 37 months one second malignancy occurred (thyroid cancer).

Treatment failures in the Stanford V patient group were mostly due to disease progression during and early after completion of chemotherapy, while the 3-year disease-free survival for patients obtaining complete remission was 85±8% for the Stanford V group in comparison to 90±4.7% for the ABVD group (p=0.447) (Table 2). There was a trend towards a better overall survival for patients treated with ABVD rather than the Stanford V regimen (96% and 91% at 3 years, respectively; p=0.07) (Figure 1). The estimated probability of freedom from treatment failure (FFTF) at 3 years was 66% for patients treated according to the Stanford V regimen and 76% for conventionally treated patients (p=0.11) (Figure 1). Prognostic factors predicting a poor outcome in patients treated with the Stanford V regimen were the presence of bulky disease (p=0.046) and histological grade 2 nodular sclerosis type of lymphoma (p=0.012).

Our data compare unfavorably with those reported by the Stanford group.[2,3] One possible explanation for this difference may be the modification of the chemotherapy regimen we had introduced by substituting mechlorethamine with cyclophosphamide. Efficacy of the MOPPEBVCAD regimen in patients with advanced Hodgkin's lymphoma was reported to be reduced when the alkylating agents lomustine and melphalan were replaced by cyclophosphamide and etoposide, indicating that substitutions may not be equivalent.[5] However, the most striking difference is the rate of consolidation radiotherapy. At Stanford, 86% of patients received radiotherapy.[2,3] In our treatment program, radiotherapy was planned only to sites of initial bulky disease > 5 cm and to sites of partial remission. As a consequence, only 56% of our patients were scheduled to receive radiotherapy, and 44% of the patients were actually irradiated.

Our data are in line with two other reports comparing abbreviated regimens with conventional treatments. In an Italian multi-center randomized study the failure-free survival rate at 3 years for patients in the Stanford V group was 53.4% compared to 81.4% for the ABVD group.[6] Along the same line, the British National Lymphoma Investigation (BNLI) study group reported better treatment results for patients treated with 6 monthly cycles of a hybrid regimen, ChlVPPP/EVA than for those treated with 11 weekly cycles of VAPEC-B, a regimen with remarkable similarity to the Stanford V program.[7] In both studies, the proportion of patients receiving consolidation radiotherapy was lower

Table 1. Patients' characteristics, treatment outcome and survival rates.

	Stanford V n = 32	*ABVD n = 64*
Age		
Median (years)	32	31
Range (years)	18 – 65	14 - 67
> 50 years (%)	15.6	17.2
Male sex (%)	62.5	50
Histologic subtype (%)		
Nodular sclerosis	68.8	70.3
NS 2	18	
Mixed cellularity	8	20.3
Other/not classified	9.4	9.4
	21.8	20.3
Clinical stage (%)		
II	46.5	48.5
III	31.3	34.4
IV	21.8	17.2
Bulky disease (%)	50	48.4
International prognostic index (%)		
0-1	29	42
2-3	52	46
4-7	19	12
Complete Remission (%)	62.5	70.3
Early failure (no change/progression) (%)	15.6	7.8
Disease-free survival (%)	85 (60-95)	90 (75-96)
Freedom from treatment failure at 3 yrs (%)	66 (47-79)	76 (63-85)
Overall survival at 3 yrs (%) (73-97)	91 (87-99)	96

The IPI score was calculated according to Hasenclever et al.[8] 95 % CI are shown in brackets.

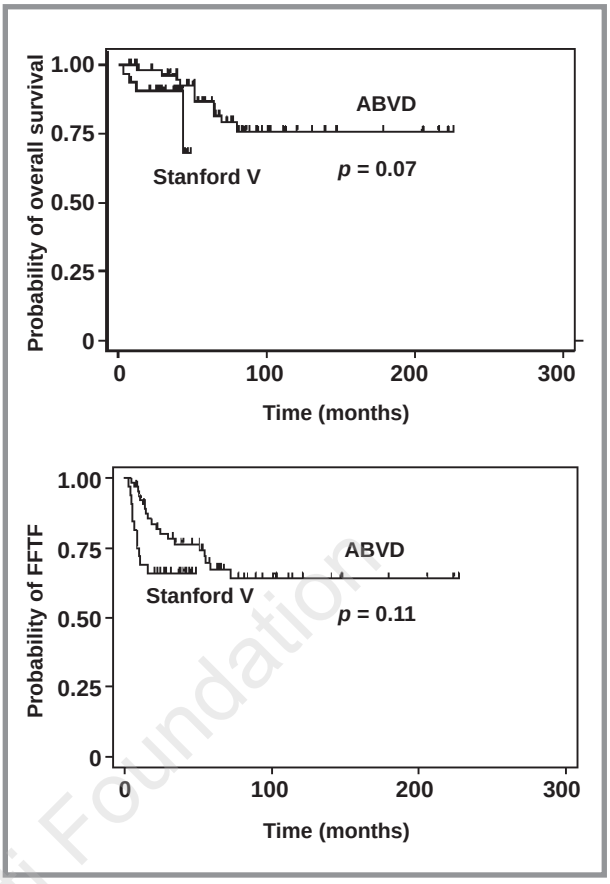

Figure 1. Kaplan-Maier analysis of (A) overall survival and (B) freedom from treatment failure (FFTF) for patients treated with the Stanford V regimen (32 patients) and with conventional treatment (64 patients). Overall survival was defined as the time from start of treatment to death or last follow-up. FFTF was calculated from start of treatment to disease progression, relapse or last follow-up. Disease-free survival was defined as the time to relapse for patients achieving complete remission. *p* values were calculated using the log-rank test All computations were performed using Stata7 software (Stata Corp., College Station, TX, USA).

than that in the group treated Stanford radiotherapy policy.[6,8]

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Key words: modified Stanford V, ABVD, Hodgkin's lymphoma.

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