if we consider only pts treated with the API-AI protocol in AD. The results observed with this non containing MTX regimen have to be validated by a large multicenter study and consecutively tested in teenegers.

Adult leukemia/Lymphoma

316 POSTER

Gender plays an important role in prognostic power of tumor distribution pattern in b-chronic lymphocytic leukemia (B-CLL).

B. Jaksic[1], O. Jaksic[2], F. Morabito[3], M. Brugiatelli[3]. [1] *University Hospital "Merkur", Medicine, Zagreb, Croatia* [2] *University Hospital "Dubrava", Medicine, Zagreb, Croatia* [3] *Azienda Ospedaliera "Bianchi-Melacrino-Morelli", Hematology, Reggio Calabria, Italy*

Purpose: B-cell chronic lymphocytic leukaemia (B-CLL) has highly variable clinical presentation, course and prognosis. In order to evaluate the impact of tumor cell distribution pattern on clinical course, the prognositic analysis was performed on 341 B-CLL patients.

Design and Methods: we introduced the model for tumor distribution (TD) assesment based on Total Tumor Mass (TTM) scoring system, where TD value represents percentage of total tumor mass infiltrating peripheral blood and bone marrow (TD=TM1/TTM). TD can be categorized into 3 subgroups: "pure leukemia" if TD=100%, "predominantly leukemia" if TD=50%-99% and "predominantly lymphoma" TD<50%.

Results: We found following distribution pattern among 341 B-CLL patients: 22.6% were "pure leukemia", 56.0% "predominantly leukemia" and, 21.4%, "predominantly lymphoma" cases, with a median overall survival of 95, 61 and 36 months respectively (p<0.0001). TD parameter significantly correlates with TTM size, Rai and Binet stages, spleen size, beta-2 microglobulin, but failed to correlate with age, lymphocyte count, soluble CD23, and bcl-2/bax ratio. Highly significant association of DT with prognosis was found in overall population of B-CLL patients (p<0.0001). However, to our surprise, both in univariate prognostic analyses and in multivariate Cox analysis this effect is much stronger in female patients, while virtually failing in male patients. In female patients DT is the strongest independent predictor of prognosis (p=0.000) followed by age (p=0.058), and Binet stage (p=0.026).

Conclusions: Tumor mass distribution pattern, a quantitative and simple clinical parameter is independent and strong prognostic parameter in B-CLL. Unexpected finding of substantial difference in prognostic power of DT between genders points out to an interesting, yet unexplained biological impact of gender in pathogenesis of B-CLL.

Adult Hodgkin's lymphoma

317 POSTER

Cardiopulmonary response to exercise in patients cured with chemo-radiotherapy for Hodgkin's disease

F. Villani[1], V. Bonfante[2], A. Fede Catania[1], C. Materazzo[3]. [1] *Istituto Nazionale Tumori, Pneumology, Milan, Italy;* [2] *Istituto Nazionale Tumori, Medical Oncology, Milan, Italy;* [3] *Istituto Nazionale Tumori, Cardiology, Milan, Italy*

Purpose: Combined CT and RT, including the mediastinum, can produce subclinical and cardiac toxic effects. From 1998 we evaluated cardiopulmonary response to exercise in pts with HD treated with this combined modality and in complete remission after >5 year follow-up.

Methods: The study was performed in 94 pts, M/F 40/54, mean age 36 yr (range 21-65). Initial stage was I in 7 pts, II in 73 pts, III in 3 pts and IV in 11 pts. CT regimens included ABVD in 56 pts, MOPP/ABVD in 10 pts, VEBEP (Vepesid, Epirubicin, Bleomycin, Cyclophosfamide, Prednisone) in 28 pts. The median cumulative dose administered was 77 mg/sqm for Bleomycin, 160 mg/sqm for Doxorubicin and 313 mg/sqm for Epidoxorubicin. The median RT dose delivered to the mediastinum was 34.4 Gy, range 27-44. Before exercise test pts were divided into 3 groups according to lung function parameters: group 1 (52 pts) with normal values; group 2 (33 pts) with total lung capacity (TLC) normal, but transfer lung factor for CO (DLCO) < 80% of predicted; group 3 (9 pts) with both spirometry and DLCO <80% of predicted. The median drugs and RT doses received by these 3 groups of pts were similar. Pts were submitted to respiratory and arterial blood gasses analysis, determination of cardiac output (acethylene rebreathing method) before and during a symptom limited exercise on cycloergometer using an incremental protocol. Expiratory gasses were analyzed by a mass spectrometer.

Results: Pts of groups 2 and 3 in comparison with those of group 1 showed a lower oxygen consumption (VO2 max: group 1 vs group 2 and vs group 3: 59.3%, vs 58% vs 52.5 of predicted) and a significant lower cardiac output per oxygen uptake.

Significant correlations were observed between basal TLC, stroke index and VO2 max.

Conclusions: These data show a reduction of the physiological response to exercise in pts with pulmonary impairment after CT-RT, in particular when the reduction of DLCO is associated with modification of spirometric parameters.

This lower capacity to exercise seems to be due to a combination of lung impairment for gasses diffusion and to a reduction of myocardial function with decrease of stroke volumes.

318 POSTER

Early Hodgkin's disease: treatment without radiotherapy

P. Provencio[1], P. España[1], I. Millan[1], A. Sanchez[1], B. Cantos[1], M. Yebra[2], J. Vargas[2], F. Roman[2], C. Miralles[1], B. Bonilla[1]. [1] *Clinica Puerta De Hierro, Medical Oncology, Madrid, Spain;* [2] *Clinica Puerta De Hierro, Internal Medicine, Madrid, Spain*

The treatment of choice for patients with early stage Hodgkin's disease (HD) has been extended field or subtotal nodal irradiation. Remission rates of over 95% have been obtained, however, about 5% of stage I and II patients will suffer from progressive disease while on therapy and an additional 15% - 20% will relapse. Chemotherapy (CT) alone has not been adequately tested in early-stage HD.

Patients, methods and results: All HD stage I and II patients treated with CT alone between 1980 and 1997 were reviewed. Thirty-five patients were treated between 04/80 and 12/97. All patients achieved complete remission. The median follow-up was 119 months (range 21-240 months), no patients were lost at follow-up. Overall survival was 97% (IC 95%, 92-100) at 5 years and 88% (IC 95%, 75-100) at 10 years. Failure free survival was 93% (IC 95%, 83-100) at 5 years and 66% (IC 95%, 47-86) at 10 years. Three (8.5%) patients died: 2 due to a second tumour (non-Hodgkin's lymphoma and myeloid acute leukaemia) and the other due to sepsis post-Ch. Univariate and multivariate analysis only associated histology subtype relative risk 4.0 nodular sclerosis (95% IC, 1.0 - 5.5; p:0.02) with higher relapse. Other prognostic factors did not reveal significant differences with respect to failure free or overall survival.

Conclusions: We believe than death from HD in early-stage patients is unusual and mortality from causes other than HD occurs many years later. Outside clinical trials due to the lack of clear prognostic factors, with the exception of specific situations, patients should be informed of all the possible alternatives as well as the consequences of the treatments employed. In our experience it appears that using CT alone in the initial stages does not jeopardise overall patient survival, with similar results being achieved.

319 POSTER

Feasibility of the integration of Stanford V ct regimen with highly active antiretroviral therapy (HAART) and G-CSF in patients (pts) with HD and HIV infection (HD-HIV)

M. Spina[1], J. Gabarre[2], E. Vaccher[1], A. Re[3], A. Palmas[4], A. Antinori[5], M. Clerico[6], U. Tirelli[1]. [1] *National Cancer Institute, Medical Oncology A, Aviano, Italy;* [2] *Pitié-Salpetrière, Hematology, Paris, France;* [3] *Civil Hospital, Oncology, Brescia, Italy;* [4] *Civil Hospital, Oncology, Nuoro, Italy;* [5] *Spallanzani Hospital, Oncology, Rome, Italy*

The outcome of pts with HD-HIV is still poor, mainly because the duration of complete remission (CR) is quite short. In order to try to improve the prognosis of HD-HIV, a feasibility study with the intensive 12-week CT regimen with adjuvant radiotherapy, Stanford V and concomitant HAART was started in previously untreated HD-HIV pts with bulky limited stage or stage III-IV. Pts were treated with CT(mg/mq) including doxorubicin 25 and vinblastine 6 on wks 1, 3, 5, 7, 9, 11; nitrogen mustard 6 wks 1, 5, 9; etoposide 60 x 2 wks 3, 7, 11; vincristine 1.4 (max 2) and bleomycin 5 wks 2,4,6,8, 10, 12 and prednisone 40 qod. Since April 1997, out of 49 pts entered, 46 are now evaluable for toxicity and response. The median age was 36 yrs (range 28-63). All pts but 5 were males, 20 were IVDUs, 14 homosexuals and 12 heterosexuals. The median CD4+ cell count at entry

was 225/mmc (range 32-1008) and 27 pts had a detectable HIV viral load (median 3600 copies/mmc (range 60- 455000). Stage III and IV disease was present in 33/46 (72%) pts. Histologic subtypes were: MC 43%, NS 24%, LD 6%, not determined 26%. As far as toxicity, no toxic death was observed, while an absolute neutrophil count <500 was observed in 37 out of 46 pts (80%). Grade 4 anemia was observed in 20/46 pts (43%) and severe thrombocitopenia in 8/46 (17%) pts. Thirteen pts (28%) had febrile neutropenia with 3 documented bacterial sepsis. A grade 2-3 peripheral neuropathy was observed in 15/46 pts (33%). CR was obtained in 37/45 pts (82%) and PR in 4/45 pts (9%). Seven CR pts relapsed (19%). The actuarial overall survival and disease free survival at 2 years are 57% and 66%, respectively. Our preliminary data demonstrated that the abbreviated CT regimen, Stanford V, in combination with HAART is feasible and active in pts with HD-HIV. Supported by AIRC and ISS grants.

320 POSTER

Outcome of very late relapse of Hodgkin's disease (HD) at the National Cancer Institute of Milan

S. Viviani[1], V. Bonfante[2], F. Lussana[3], A. Di Russo[4], P. Valagussa[5], G. Bonadonna[6], A.M. Gianni[7]. *[1] Istituto Nazionale Tumori, Medical Oncology, Milan, Italy; [2] Istituto Nazionale Tumori, Medical Oncology, Milan, Italy; [3] Istituto Nazionale Tumori, Medical Oncology, Milan, Italy; [4] Istituto Nazionale Tumori, Radiotherapy, Milan, Italy; [5] Istituto Nazionale Tumori, Medical Oncology, Milan, Italy*

Purpose: HD is a highly curable neoplasm,however very late relapse, occurring more than 10 years after achieving CR with first line therapy,is rare but not uncommon.We report the outcome of 13 pts relapsing more than 10 years after CR.

Methods: Among 523 pts enrolled at our institution in prospective studies and in CR after first line treatment 13 pts(2.5%)relapsed after a median of 179 months (range 123-216).Main pt characteristics at relapse were as follows:median age 40 years(range 29-66);males/females 9/4;stage I+II/III+IV 6/7;B symptoms 2.Treatment at relapse was:RT alone in 1,ABVD in 2,MOPP/ABVD in 8,MOPP in 1 and Vinorelbin+Prednisone in 1 case.Consolidation RT on nodal involved and not previously irradiated sites was delivered at the end of chemotherapy(CT) in 6 pts.

Results: Eleven pts (85%) achieved a 2nd CR,while 2 pts failed.Eight pts (64%) are alive and disease-free after a median of 84 months (range 26-180) from start of salvage CT,one pt relapsed subsequently and was salvaged by high-dose CT+PBSC reinfusion,for a total of 9 pts (69%) alive at 61 months (range 26-180).Two pts died in CR from HD:one for heart failure and one for metastatic gastric cancer.One pt,aged 66 years and in continuous CR,developed a myelodisplasia 26 months after the end of second line therapy.

Conclusion: This study confirms that the percentage of pts relapsing more than 10 years from the end of first line treatment is very low (2.5%).Taking into account the long event-free survival experienced by 61% of our pts,we suggest that conventional-dose salvage CT should be the treatment of choice in this favorable subset of HD pts with very late relapse.

321 POSTER

Analysis of second cancers following Hodgkin's disease treatment

H. Eghbali[1], S. Mathoulin-Pélissier[2], V. Picot[2], R. Tabrizi[1], P. Soubeyran[1], B. Hoerni[1]. *[1] Institut Bergonie, Hematology, Bordeaux, France; [2] Institut Bergonie, Biostatistics, Bordeaux, France*

Introduction: Cardiovascular complications and secondary cancers after Hodgkin's disease (HD), concern more than any other side-effect because of their direct impact on the survival. Both are linked to radiotherapy and limiting its role in the cure of HD is under investigation. But however the role of other factors has to be underlined such as smoking, alcohol, thyroid impairment, female hormonal status and occupational exposition or immunosuppression.

Method: We carried out a retrospective study of all second cancers in a cohort of HD treated in our institution and analysed factors favouring second cancers, assuming that in our centre we never performed staging laparotomy, but combined modality treatment.

Results: Among 920 patients treated since 1960 and with a median follow up of 11.5 years (min 2- max 38) 76 cases of second cancers were detected.

Most of them occurred in irradiated areas confirming the role of radiotherapy. But some were far from radiotherapy fields in urinary tract (kidney, bladder, ureter, gall bladder, colon and lymphomas) suggesting the role of either chemotherapy or some other factors. The median time to second cancer is 141 months and the survival since its occurrence shows a 5-year overall survival of 25% indicating that this complication remains highly life threatening and deserves prevention by a more adapted treatment for initial HD.

Cancer type	Number (%)
Non Hodgkin's lymphomas	13 (17.1)
Lung or throat cancers	10 (13.2)
Renal or urothelial carcinomas	6 (8)
Digestive carcinomas	7 (9.2)
Thyroid carcinoma	4 (5.2)
Breast cancer (among 338 females)	9 (12)
Skin carcinoma & melanoma	4 (5.2)
Sarcomas	4 (5.2)
Acute leukaemia	12 (15.8)
Undetermined origin	4 (5.2)
Miscellaneous (brain, ovary)	3 (4)

322 POSTER

Hodgkin's disease among patients older than 60

H. Eghbali[1], V. Picot[2], S. Mathoulin-Pelissier[2], R. Tabrizi[1], P. Soubeyran[1], B. Hoerni[1]. *[1] Institut Bergonie, Hematology, Bordeaux, France; [2] Institut Bergonie, Biostatistics, Bordeaux, France*

Introduction: Old patients (pts) with Hodgkin';s disease (HD) are usually excluded from trials and information for such pts are rare. Many publications stressed that HD of the elderly may be a different entity, which explains the poorer prognosis. Old patients have usually a lot of comorbidity, limiting curative chemotherapy.

Method: We analysed clinical characteristics of old pts with two limits to define the elderly: over 60 and over 70 years dispatched in three cohorts of <60, 60 to 70 and >70. Initial characteristics concerning sex, stage, mediastinum, pathology, biological data, treatment and results were reviewed.

Results: Among 912 pts with more than 3 years follow up, 128 were over 60, 70 between 60-70 and 58 over 70. Sex ratio was similar to that of the young (ns). Histology type 3 was significantly more frequent (50% vs 30%, P=0.0001) and mediastinum involvement was less frequent with a linear association with age (p value<0.000001). Bulky disease, percentage of limited or extended stages, systemic symptoms, E-extension or compressive behaviour were in the same percentage than among young pts (ns in all comparisons). Treatment strategy was similar to that of the young HD with combined modality treatment for stages I & II and chemotherapy alone for extended stages, 10% of patients had radiotherapy alone. Analysis of response failed to show a difference between the young and the old in term of complete remission. For relapse, there is no difference between group 60-70 year and the young (19.4% vs 18%), but there are more relapses for the very old (38% vs 19.4%, p=0.0007) when compared to the younger groups. 5 year overall survival is not very good (40%, 60% and 90% according to age) the specific survival including only HD and treatment toxicity related deaths displays a better survival (63% vs 75% vs 89% respectively).

Conclusion: According to this study there is not major difference between young and old HD excepting histology and medistinum involvement. The primary treatment response is roughly the same. However the higher rate of relapse and a worse cause specific survival may reflect the fact that these patients has not the necessary amount of chemotherapy and justify a specific and adapted regimen for these pts.

323 POSTER

Prospective randomized trial in the treatment of early stage hodgkin's disease (ESHD) using involved field radiation therapy (IFRT) vs. subtotal nodal irradiation (STNI) after a short chemotherapy (CT) course

A. Di Russo[1], V. Bonfante[2], S. Viviani[2], L. Devizzi[2], A. Santoro[2], M. Zanini[1], F. Soncini[1], F. Villani[3], P. Valagussa[2], G. Bonadonna[2]. *[1] Istituto Nazionale Tumori, Radiotherapy, Milano, Italy; [2] Istituto Nazionale Tumori, Medical Oncology, Milano, Italy; [3] Istituto Nazionale Tumori, Cardiology, Milano, Italy*

Purpose: The aims of this prospective, monoinstitutional trial are to evaluate: a)whether or not short course CT (ABVD 4 cycles) plus RT improves the freedom from progression (FFP) and the overall survival (OS) rates in