796 POSTER

DISTANT RESULTS OF SURGICAL TREATMENT OF PRIMARY GI-TRACT NHL ADULTS

I. Poddubnaja
Oncology Chair, Cancer Research Center of RAMS, 115478, Moscow, Russia

GI-tract is most frequent extranodal lesion of NHL—14.5%. 30-years study (1985–1994) 488 pts with NHL of GI-tract was done. Lesion frequency of different part of GI-tract is: stomach (st.)—59%, small intestine (sm.int.)—26%, colon (col.)—7.5%. Simulations lesion of several parts GI-tract is registered only in 7.1%. Predominance B-cell high grade NHL is noted—78%; IE stage—17%, IIE—40%, IIIE-IV—43%. Initially limited spread in almost 1/2 of pts and tendency to regional spread (71%) led to well-grounded surgical treatment. Radical operations were made: st.—74%, sm.int.—23%, col.—52%. 5-year survival—78%, 77%, 66% of st., sm.int., col. (respect.). 10-year survival is almost the same: 63%, 76%, 65% (respect.). Analysis of relapse free survival (RFS) had shown that best results are registered with st.: medians RFS—86 mths in comparison to 25 mths in any part of intestine. 5-year RFS are—58.3%, 28.5%, 24.8% (st., sm.int., col. respect.). RFS is registered in 1/4 pts (24–29%). Adjuvant chemotherapy (Ad.chem.) till 1985 was used during 1.5 year (COP every 1.5 mths). We gained insignificant increase of RFS. Later Ad.chem. considered of 2–3 cycles (COP, CHOP, LVPP) with poor prognostic factors present. Preliminary results led us speak about increasing of 3-year RFS on 11%. Registered high frequency of serious complications (st.—25.8%, sm.int.—53.7%, col.—44%), low efficacy of chemotherapy—25.9% (CR—9.9%, PR—16.4%) proved operation to be rather effective treatment of IE-IIE stages GI-tract NHL. Results of Ad.chem. are being specified.

797 POSTER

SINGLE CENTRE RESULTS OF THERAPY INCLUDING AUTOGRAFTS IN PREVIOUSLY UNTREATED MYELOMA

R. Powles, N. Raje, T. Hickish, G. Middleton, S. Milan, J. Mehta, S. Singhal, C. Viner, J. Treleaven, D. Cunningham
The Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT, U.K.

Autografting became part of our myeloma treatment strategy in September 1986. Since then until March 1994, 195 new untreated patients between the ages of 30 and 70 years received induction chemotherapy with either VAMP, C-VAMP or V-C-VAMP. The complete remission (CR) rate following induction was 18%. 144 (74%) of these patients went on to receive high dose (HD) treatment (Busulfan or Melphalan), of which 110 (56%) received high dose melphalan plus an autograft. Analysis is as of December 1994 with a median follow up of 41 months. Among the 110 patients, 89 received bone marrow while 21 patients were rescued with peripheral blood stem cells. The complete remission rate after HD in this group of patients was 74.5%. 21% achieved a partial remission and there were only 3 non-responders. There was 1 (0.9%) transplanted related death and therefore response could not be evaluated.

The actuarial overall survival of the above transplanted patients by the Kaplan Meier estimate was 52.7% at 6 years and 50% of the patients remained progression free at 29 months. Fifty-seven patients have progressed to date and 33 have died. All but one death are due to disease progression. Sixty-eight patients subsequently went on to maintenance Interferon. Analysis of the total series of 195 patients shows a complete remission rate of 54% (104/195) with 35% of the complete responders surviving at seven years. We thus conclude that cytoreductive treatment followed by high dose chemotherapy produces high remission rates which in turn results in improved survival. Interferon has been shown to be effective in maintaining remission and has been incorporated as maintenance treatment. This should therefore be first line treatment in young myeloma patients.

798 POSTER

PROGNOSTIC FACTORS IN MULTIPLE MYELOMA

N. Raje, R. Powles, S. Milan, J. Mehta, S. Singhal, C. Viner, J. Treleaven, D. Cunningham
The Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT, U.K.

Follow up data of 204 Myeloma patients seen at the Royal Marsden were analysed for factors predicting the overall survival. All these patients were newly diagnosed and went on to receive VAMP/C-VAMP/V-C-VAMP, infusional cytoreductive treatment. 146 of these patients received some form of high dose treatment (Melphalan or Busulfan). A Cox regression analysis was carried out on clinical and laboratory factors just prior to treatment. Multivariate analysis revealed stage ($P = 0.0001$), Hb ($P = 0.03$), serum Calcium ($P = 0.01$) and performance status ($P = 0.01$) as independent prognostic factors. Beta2 microglobulin was however not included in this analysis as this was not done routinely in the initial patients (n = 51). When however we repeated the analysis after the elimination of these 51 patients, Beta2 microglobulin was the single most important prognostic variable ($P < 0.0001$). We then looked at the same prognostic variables in the 146 patients who received high dose treatment and found only Hb ($P = 0.03$) and serum Calcium ($P = 0.02$) emerging as independent prognostic variables. On repeating the analysis on those who had Beta2 microglobulin estimation, this was again the only variable which was independently significant ($P = 0.001$). This therefore illustrates the point that the prognostic value of different variables may be influenced by successful treatment. We conclude from the above data that pretreatment Beta2 microglobulin, serum calcium and haemoglobin affect the overall survival in myeloma patients in spite of aggressive treatment.

799 POSTER

VAMP/C-VAMP INFUSIONAL CHEMOTHERAPY AS INDUCTION TREATMENT FOR PREVIOUSLY UNTREATED MULTIPLE MYELOMA

N. Raje, R. Powles, T. Hickish, M. Gore, S. Milan, J. Mehta, S. Singhal, C. Viner, J. Treleaven, D. Cunningham
The Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT, U.K.

204 previously untreated Multiple Myeloma patients received a four day infusional chemotherapy schedule with Vincristine, Adriamycin, Methyl prednisolone with the addition of Cyclophosphamide and/or Verapamil as outpatient treatment as part of their induction therapy in the study period between April 1985 and March 1994. The aim of this treatment was to reduce tumor burden and marrow infiltration prior to high dose therapy. The objective of this analysis was to ascertain response to cytoreductive treatment prior to autografting and to see if addition of Cyclophosphamide and/or Verapamil influenced response. Among the 204 patients, 91 received C-VAMP chemotherapy, 75 received VAMP and 38 patients received Verapamil in addition to C-VAMP. The median number of courses to achieve maximum response in the whole group was 5 (range 1–11). The overall response to induction treatment was 71.0% (144/204) with 18.0% (37/204) achieving a complete response (CR). The response in the three subsets of patients is shown in the following table.

Induction treatment	No. patients	CR (%)	*P* value
VAMP	75	6 (7.9%)	
C-VAMP	91	22 (24%)	0.04
V-C-VAMP	38	9 (23%)	

Seventeen patients have died during induction with 4.0% (9/204) deaths as a result of induction treatment. We therefore conclude that a median of 5 courses of cytoreductive treatment is required for maximum response. The CR rate with just cytoreductive treatment is low and requires consolidation with high dose treatment and autografting. The addition of Cyclophosphamide to VAMP alone produces significantly better responses. The addition of Verapamil to the C-VAMP has not made any difference to outcome.

800 POSTER

CONTIGUOUS SPREAD IN LYMPHOGRANULOMATOSIS IN 297 PTS

S.L. Roth, H. Sack, K. Havemann, H. Stüzer
University of Duesseldorf, Essen, Marburg, Germany

Purpose: The hypothesis is tested in 297 patients with Hodgkin's disease, that it does arise in one site and spreads in a predictable manner in the lymphatic system before hematogenous dissemination.

Materials and methods: 70 PS I, 66 PS II, 137 PS III. and 15 PS IV Hodgkin's disease patients. 188 A, 109 B. 236 presented cervical lymphomas: 80 left-, 92 right- and 64 bilateral-cervical. They were grouped according to the number of involved sites.

Results: A characteristical pattern was observed in 88%. The accuracy of the hypothesis is significant for the 236 patients with cervical lymphoma ($P = 0.01$; T-test).

Conclusion: HD spreads from the right cervical side via the upper mediastinum and hili to the upper abdominal nodes and the spleen whereas left cervical lymphoma leads to direct abdominal involvement bypassing

the mediastinum. Abdominal involvement precedes upward spread via the pulmonary hili and upper mediastinum on the left side or on both sides to the cervical or axillary or inguinal nodes.

801 POSTER

SECOND AUTOGRAFTS FOR RELAPSED MYELOMA

S. Singhal, R. Powles, D. Cunningham, T. Hickish, G. Middleton, N. Raje, C. Viner, J. Mehta

Royal Marsden Hospital, Surrey, U.K.

Forty-four pts (34–64 y, med 47.5) underwent second autografts for relapsed myeloma 10–99 mo (med 33.5) after the first. All received high-dose melphalan and BM (43 auto, 1 twin) the first time. 30 received high-dose melphalan, 10 busulfan, and 4 TBI for the second. The source of cells was BM (29 auto, 1 twin) or blood stem cells (n = 14). At the time of the second transplant, 2 pts were in CR, 21 in PR, and 21 had progressive disease. Hematologic recovery was complete in all pts after the first transplant, but not after the second. 12 pts died of toxicity at 0.5–5 mo (med 1). 16 died of progressive disease or toxicity of further therapy 2–54 mo (med 16) later. 10 pts attained CR after transplant. The probability of progression-free survival at 3 years is 8.9% (95% CI: 1.8–23.5%). 14 pts were started on IFN-α 1.5–9 mo (median 2.5) after the second transplant before any evidence of disease progression. 16 pts, 12 on IFN-α, are alive 1.5–66 mo (med 10.5) after the second transplant: 2 in continuous CR, 7 in stable PR, and 7 with progressive disease. The overall survival of this group was not different from a group of 60 relapsed patients who did not undergo repeat transplants. We conclude that although repeat autografts are feasible in relapsed myeloma, it is difficult to show an improvement in survival and the exact place of second transplants remains to be defined.

802 POSTER

DOSE INTENSITY (DI) CHEMOTHERAPY IMPROVES DISEASE FREE SURVIVAL IN ELDERLY AGGRESSIVE NON-HODGKIN'S LYMPHOMA (NHL) PATIENTS TREATED WITH CONVENTIONAL CHOP

H. Gómez, S. Santillana, L. Casanova, S. Valdivia, J. Otero, L. Mas, C. Vallejos

M.D. Instituto de Enfermedades Neoplásicas Lima, Perú 1995

Aggressive NHL in elderly pts remains a problem when are treated with suboptimal chemotherapy dosage; however the exact role of CHOP dose intensity in the outcome of these pts. has not been fully addressed.

Between 1982 and 1993, 284 pts with intermediate and inmunoblastic NHL, older than 60 years old were admitted to receive conventional CHOP for 6 courses or until progression; 171/284 were evaluable for response and toxicity.

The F/M ratio was 1:1.25 with a median age of 69 years (61–84). The histology was WF:G 95/171, WF:H 31/171 and WF:E 20/171. According to the International Index 59/171 (34%) were Low Risk; 64/171 (37%) Low-Intermediate, 34/171 (20%) High-Intermediate and 14/171 (8%) High risk group. There were 10/171 toxicity-related deaths and five deaths due to disease progression (5) during the treatment. Sixty-two percent of the pts. (107/171) achieved complete response (CR).

All patients were stratified in two groups according to a Relative dose intensity RDI (mg/m^2/week) in two groups: A) $\geq$ 80% and B) $\leq$80%. No CR rates differences were noted between two groups. With a median follow up of 30 months, the two-year disease free survival (DFS) was similar in two groups, except for the low intermediate risk in favor of the high RDI group (81% vs 45%, $P = 0.002$). A benefit in the 5 year-overall survival (DS) was also observed in both intermediate risk groups (69% vs 30% and 44% vs 0%, $P = 0.002$). These data suggest a survival benefit in at least two subsets of elderly NHL pts who received $\geq$ 80% R.D.I. of CHOP, showing the advantage of the DI concept in elderly LNH pts.

803 POSTER

RADIOTHERAPY SALVAGE FOR HODGKIN'S DISEASE AFTER CHEMOTHERAPY FAILURE

A. Wirth, J. Corry, K.H. Liew

Department of Radiation Oncology, Peter MacCallum Cancer Institute (PMCI), Melbourne, Australia

A retrospective study was performed at the PMCI to assess the effectiveness of radiotherapy (RT) as sole salvage treatment for relapsed Hodgkin's disease (HD). Between 1978 and 1992, 52 patients with relapsed/ refractory HD following chemotherapy (CT) received RT with curative intent. Patient characteristics at diagnosis: median age 26, with 32% > 40 years old; M/F 31/21; stage I-4,II-16, III-25, IV-7. Initial CT was MOPP- 31 patients, ABVD-1, both-16. A median 6 cycles of CT was given per regimen. Prior to salvage RT, 26/52 patients had received both MOPP and ABVD, either as sequential regimens, or as alternating or hybrid protocols. The response to initial CT was: CR-30, PR/SD-18, PD-4. Duration of initial CR was < 12 months in 8/30 patients. Salvage treatment consisted of radiotherapy to all known areas of disease. Doses ranged from 3600–4000 cGy. Twenty three patients (45%) achieved CR. With a median follow-up of 70 months (range 4.8–166), actuarial median failure free survival (FFS) and overall survival (OS) are 22 months and 83 months respectively. Actuarial 5 year FFS and OS are 26% and 57% respectively. Patients with CR duration >12 months following initial CT, only one CT regimen prior to salvage RT, and anatomically limited relapse had a significantly longer FFS. These factors, and age <40 were associated with significantly longer OS. Only 6% of patients failed solely in the irradiated volume as first site of relapse. Salvage RT was well tolerated and resulted in no treatment-related deaths. RT is of benefit in selected patients, and should be considered as a treatment option for patients with HD who fail CT.

804 POSTER

EPSTEIN-BARR VIRUS AND HODGKIN'S DISEASE: COMPARISON BETWEEN ALGERIAN AND FRENCH PATIENTS

F. Zerhouni, M.I. Belkaïd, K. Beldjord[1], J. Brière[1], M. Andrieu[1], P. Colonna

Service d'Hématologie, Centre P et M Curie, Avenue Battandier, Alger 16005, Algeria

[1] Service d'Hémato-Oncologie, Hôpital laënnec, 42 rue de Sèvres, 75007 Paris, France

The prevalence of Epstein-Barr virus (EBV) markers in nodal lesions from Algerians (Al) patients (n = 68) was compared to French (Fr) patients (Pts) (n = 21) with Hodgkin's disease. Initial characteristics were: males Fr 57%, Al 53%; median age Fr 29, Al 25; histologic subtypes: lymphocytic predominance (LP) Fr 1, Al 3; nodular sclerosis (NS) Fr 16, Al 33; mixed cellularity (MC) Fr 4, Al 30; lymphocytic depletion (LD) Al 2.

The latent membrane protein (LMP) expression was founded in Reed-Sternberg cells (RSC) in 26 cases Al (1 PL, 8 NS, 17 MC) and 4 Fr (2 NS, 2 MC). All cases LMP-positive were also by DNA or RNA *in situ* hybridization (ISH). ISH was positive in RSC of 29% of Fr and 66% of Al Pts ($P < 0.02$); the positivity was more frequent in MC (80%) than in other histologic types (39%). EBV genome was detected by PCR on DNA in 84% of Fr and 95% of Al patients (100% of MC and 86% of other histologic types).

More pronounced ISH positivity in Al young adult cases ($P < 0.05$) can result from the age at primary EBV infection, which occurs earlier in Algeria than in France.

805 POSTER

VINCRISTINE, ETOPOSIDE, MITOXANTRONE AND PREDNISONE (VEMP) AS FIRST-LINE CHEMOTHERAPY FOR HODGKIN'S DISEASE (HD)

G.B. Zulian, B. Mermillod, P.A. Iten, P. Alberto

Division of Oncology, Geneva University Hospital, CH-1211 Geneva 14, Switzerland

Etoposide and mitoxantrone were combined with vinca alkaloid and steroid in order to evaluate the activity of a new combination, VEMP, whilst avoiding the long term complications related to MOPP and ABVD. 30 consecutive patients (pts) with *de novo* HD were treated between Jan. 1992 and Dec. 1994. 21 were males, median age was 34 years (range 18–67). 3 patients were HIV+. 18 had nodular sclerosis, 8 mixed cellularity, 3 lymphocytic predominance, 1 lymphocyte depletion. 2 pts were IA, 6 IIA, 3 IIB, 5 IIIA, 3 IIIB, 2 IVA, 9 IVB. 4 pts had lung involvement, 2 bone marrow, 1 liver, 1 bone, 3 both liver and bone marrow. VEMP was given on a 21-day (D) cycle basis for a median of 6 courses as follows: vincristine 1.4 mg/m^2 iv D1 and 8, etoposide 100 mg/m^2 iv D1 to 4, mitoxantrone 10 mg/m^2 D1 and prednisone 100 mg po D1 to 5. Toxicity data are available for 25 pts. 6 pts had grade (G) 4 WHO leucopenia, 18 G2, 2 G1. 1 pt had G4 infection, 2 G2, 1 G1. 1 pt had G4 thrombocytopenia, 7 G1. Peripheral neuropathy G1 occurred in 10 pts, G2 in 6. 1 pt had cutaneous erythema, 1 toxic hepatitis, 1 myocardial infarction, 1 fatigue. Response rate was 100% with 42% complete remission (CR), 20% CR unconfirmed (CRu) and 38%