Ifo 35

COMBINATION CHEMOTHERAPY WITH MITOMYCIN-C, IFOSFAMIDE AND VINDESINE IN THE TREATMENT OF NSCLC

U. Gatzemeier, D.K. Hossfeld, H. Magnussen, D. Radenbach, R. Zschaber

Introduction: The most active single agents in NSCLC are Mitomycin-C, Ifosfamide, Vindesine and cis-Platinum. DDP-Containing combinations showed a remission rate of about 40 % (own results) with high rate of toxicity. To improve results we have to look for new drug combinations with tolerable toxicity. This was the rationale for a phase-II-trial to determine the effectiveness and toxicity of the triple-drug regimen with Mitomycin-C, Ifosfamide and Vindesine.

Patients and methods: Since 3/1984 55 patients with inoperable NSCLC were entered in the study until 4/1985. 50 patients are evaluable for response and median survival time, 46 male, 9 female. Median age 60,3 years. Performance-Status more than 70 % in all patients. 38/55 patients had extensive disease. Histology: 40 squamous cell, 9 large cell, 6 adeno carcinomas. Prior chemotherapy: 9 (DDP/VP-16).

Dose schedule: Mitomycin-C 10 mg/m^2 i.v. day 1; Vindesine 3 mg/m^2 i.v. day 1; Ifosfamide 1,5 g/m^2 i.v. day 1 - 5.

Results: The response rate was 23/50 patients(46 %), 4 patients (8 %) achieved a complete remission, 19 patients (38 %) a partial remission. According to the stage we had a response rate of 68,7 % in limited disease and 35,5 % in extensive disease. Median survival time in responders is 8,5 (+) months (follow-up 6 months) and 6,5 (+) months in Non-responding patients.

The toxicity was moderate without severe problems in gastro-intestinal or hematological side effects. There wasn't a drug related death.

Conclusion: 1) The combination Mitomycin-C, Ifosfamide and Vindesine is very active in the treatment of NSCLC. 2) Remission rates are encouraging. For MST-data a longer follow-up-period is necessary. 3) The toxicity is moderate, especially to DDP-Containing combinations.

Dep. of Pneumological Oncology Großhansdorf Hospital
Wöhrendamm 80, D-2070 Großhansdorf

Ifo 36

COMBINATION CHEMOTHERAPY WITH VP-16, IFOSFAMIDE, METHOTREXATE AND BLEOMYCIN FOR REFRACTORY OR RECURRENT LYMPHOMAS

M.R. Nowrousian, B. Schoetensack, N. Niederle, Ch. Anders, S. Seeber and C.G. Schmidt

Thirty patients (pts) (5 female,25 male), ages 17-66 years (median 41), with refractory or recurrent Non Hodgkin's Lymphomas (NHL) or Hodgkin's disease (HD) were treated. Of these pts, 26 (86%) had stage IV, 3 (10%) stage III and 1 stage II of the disease at the time of diagnosis. All pts had received extensive prior chemotherapy with combinations containing Adriamycin in 20 of 30 pts. Therapy consisted of VP-16 (90 mg/m^2, Days 1,3,5), Ifosfamide (1.2 g/m^2 + Mesna, Days 1-5) and Methotrexate (MTX) (30 mg/m^2, Days 1,5). In 3 pts with CNS involvement, 1/3 of each MTX dose (=10 mg/m^2) was given i.th. In 10 pts, Bleomycin (15 mg s.c., Days 1,5,12) was given additionally and in a further 10 pts, higher dosages of MTX (50-100 mg/m^2, Days 1, 5) was applied together with Leucovorin rescue. Treatment was repeated every 3-4 weeks. The overall response rate was 83% with a complete remission (CR) rate of 30% and a partial remission (PR) rate of 53%. 3 out of 19 pts with refractory lymphomas and 6 out of 10 with relapsing diseases achieved CR. The rate of PRs was 12/19 and 4/10 respectively. 1 CR and 8 PRs were obtained in the 11 pts with HD (8 refractory, 3 relapsed). Of the 19 pts with NHL (10 refractory, 9 relapsed), 8 pts responded with CR and 8 pts with PR. The duration of CRs was 2-11+ and that of PRs 3-10+ months. Major toxicities observed in a total number of 95 therapy courses were stomatitis (6%) and septicemia (5%) occuring mainly in pts with i.th. MTX. No therapy related death was observed. On the basis of these results, VIM(B) combination appears to be an effective and well tolerated regimen in pts with refractory or relapsed lymphomas. Thus, it appears to be reasonable to evaluate the efficacy of this drug combination in relation to the primary therapy of these diseases.

Innere Universitätsklinik und Poliklinik (Tumorforschung), Westdeutsches Tumorzentrum, D-4300 Essen

Ifo 37

SALVAGE THERAPY WITH ETOPOSIDE,IFOSFAMIDE,METHOTREXATE AND BLEOMYCIN IN NON-HODGKIN'S LYMPHOMAS

B.Steinke, F.W. Busch, M.Heim, H. Arnold

18 patients with NHL (centrocytic 2, centroblastic-centrocytic 2, centroblastic 8, immunoblastic 3, high malignant, not further defined 3) resistant to first-line treatment (CHOP) entered a study using the following therapy: etoposide 100mg/m^2 iv day 1 - 3, ifosfamide 1,0 g/m^2 iv day 1 - 5, methotrexate 30 mg/m^2 iv day 3 and bleomycin 10 mg iv day 7 and 14. For prophylaxis of cystitis, uromitexan was given together with ifosfamide. Cycles were repeated in a three weeks' interval. Preliminary results of this ongoing study are as follows: 8 patients (44%) achieved a complete remission. With a median follow up of 12 months, three of these patients relapsed 6, 6, and 18 months after start of salvage therapy. 3 patients showed a partial remission. 7 patients had only a minor or no response. Median survival from start of therapy is 16 months (projected) for all patients. It is not yet reached for responders and only 4 months for non-responders. Toxicity of treatment was usually mild. In 14 % of 50 cycles analysed so far, leucocytes fell below 2000/ul. In 6 % thrombocytes dropped to less than 75000/ul. 4 series were complicated by fever which was treated by antibiotic therapy. Stomatitis was mild and seen only in 2 series. 3 patients had skin alterations similar to sclerodermia. In these cases bleomycin was stopped and the skin alterations regressed. These results show, that the combination of ifosfamide, etoposide, methotrexate, and bleomycin is an effective treatment in NEL resistant to first-line therapy. Updated data will be presented at the meeting.

Ifo 38

CHOP-RESISTANT NON-HODGKIN-LYMPHOMAS:ALTERNATIVE COMBINATION CHEMOTHERAPY WITH IFOSFAMIDE; BLEOMYCIN, ETOPOSIDE AND PROCARBAZINE (IBEP)

A. Bremer, G. Bauer

Management of malignant non-Hodgkin-lymphomas (NHL) which either relapsed or failed to attain a complete remission (CR) on front line chemotherapy remains a therapeutic challenge. In previous studies we could induce partial (PR)or minor (MR) remissions in 7/8 chemotherapy refractory NHL by combined chemotherapy with ifosfamide and etoposide. To increase the rate and quality of ifosfamide/etoposide induced remissions, we added bleomycin and procarbazine developing a 4-drug chemotherapy combination (IBEP) as alternative chemotherapy in NHL which proved to be at least resistant to CHOP. Ten patients(pts) with refractory stage IIB-IVB malignant NHL (histology:centroblastic 3 pts, lymphoblastic, immunoblastic and centroblastic/centrocytic each 2 pts, centroblastic 1pt) have been treated with 4o mg ifosfamide/kg iv. d 1-5 with mesna prophylaxis, 15 mg bleomycin im. d 1, 8, 15 and 21, 12o mg etoposide/m^2 iv. d 1, 3 and 5 and 1oo mg procarbazine/m2 po. d 1-14, repeated d 28. After 1-3 (median:2) IBEP-chemotherapy courses in 3 pts a CR and in 4 pts a PR was achieved with a median remission duration of 8 + months; in the remaining 3 pts no change was observed. If future studies will confirm the encouraging result of this pilot study, the IBEP-combination chemotherapy may represent not only an effective salvage therapy particularly of CHOP-resistant NHL, but also a potential improvement of the initial chemotherapy of NHL by alternating non-cross-resistant chemotherapy combinations.

Abtlg. für Hämatologie u. Onkologie,
Augusta-Kranken-Anstalt, Bergstr. 26, 463o Bochum