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## IL-4 EFFECT ON ADHESION MOLECULES ON THE FARAGE HUMAN B-CELL LYMPHOMA LINE

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A new lymphoma cell line, Farage, was tested as a model for regulation of cell surface adhesion molecules. Farage cells do not express surface Ig, but display CD19, CD21, CD22, CD23, CD39, CD40 B-cell antigens and various adhesion proteins, such as CD11a (LFA-1), CD29 (VLA-4), CD44, CD54 (ICAM-1), and CD58 (LFA-3). In vitro exposure to IL-4 augmented the concentrations of CD23 and adhesion proteins on the surface of Farage cells and decreased the expression of CD21. EBV-LCL responded to IL-4 by the increment of CD23 and diminution of CD21 expression with no change in the level of adhesion proteins. No significant effect on the phenotype of Burkitt's lymphoma lines was detected after IL-4 treatment. The present study indicates that IL-4 modulates the expression of adhesion molecules and differentiation antigens on transformed B cells which have a phenotype characteristic for non-germinal center B lymphocytes.

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## PREVENTION OF CHEMOTHERAPY-INDUCED ANEMIA IN PATIENTS WITH CANCER OF THE HEAD AND NECK OR ESOPHAGUS BY TREATMENT WITH ERYTHROPOIETIN

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During treatment of head and neck and esophagus cancer patients with carboplatin, 5-Fu, interferon-$\alpha$ and interleukin-2, CFII, we observed a decline in their hemoglobin values. We studied if prophylactic administration of human recombinant erythropoietin, EPO (Recormon®, Boehringer Mannheim), could prevent CFII-induced anemia. 16 patients received 100 or 200 I.U. per kg s.c. 3x per week during the first 3 cycles of CFII. Response was defined as hemoglobin values greater than minus 10% of the initial level. The median serum EPO values increased from 123 to 162 mU/ml. 3 of 6 patients who received 100 I.U. and 6 of 9 patients who received 200 I.U. responded. EPO is effective in prevention of anemia induced by CFII in head and neck and esophagus cancer patients.

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## Response to Recombinant Human Erythropoietin (rHuEpo) in Patients with Cancer-related Anaemia.

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Anaemia is a frequent finding in patients with malignancies and is related to different causes, including defective responsiveness to endogenous erythropoietin and blunted erythropoietin production capability. We administered rHuEpo to 15 patients with solid tumors and secondary anaemia. The drug was given subcutaneously 5 days per week at escalating doses (75 to 150 U/kg per day): the aim was to reach and maintain a Hb level $\geq$ 10 g/dl without blood transfusion. Along with the clinical trial we evaluated endogenous Epo production through serum Epo levels and erythroid marrow activity by means of serum transferrin receptor (TfR). Half of the patients studied showed defective Epo production. Twelve patients responded to treatment with steady increases of Hb levels above 10 g/dl (mean increase of Hb: 3.6 -range 1.5-5.8), and the median dose of rHuEpo required was 75 U/kg. Treatment improved performance status and sense of well-being in 5/12 responders. Response was associated with an early increase in serum TfR. *Conclusions.* rHuEpo can stimulate erythroid marrow activity in these patients and marrow response can be adequately monitored by serum TfR. Although rHuEpo can improve the anaemia of cancer, the decision to treat should be individualized, looking more at the quality of life and cost-effectiveness than at cosmetic increases in the hemoglobin level.

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## Reduction by granulocyte-macrophag colonystimulating factor (GM-CSF) of hematologic toxicity induced by high-dose chemotherapy in patients with metastatic breast cancer.

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Twenty patients with recurrent metastatic breast cancer treated with high-dose myelosuppressive antineoplastic drugs (Cyclophosphamide 2,5 g/m$^2$ or Epirubicin 130 mg/m$^2$ both q 3. weeks) as first or second line chemotherapy were randomized in a prostective study to GM-CSF (n=11) 5 microg/kg/day for ten days after cessation of chemotherapy or control (n=9). Compared to the control-group highly significant reduction in granulocyte nadir duration (two days (0-5) with GM-CSF vs. seven (2-11) days) and seve-rity (WBC 0.4 x 10$^9$/l with GM-CSF vs. 0.2 x 10$^9$/l) was found. No difference in frequency of neutropen fever or antibiotic use could be observed.
Even though the patients treated with GM-CSF at random were more heavily pretreated with chemotherapy, there was a surprisingly higher responserate in these patients as compared to the control-group, namely 64% vs. 22%, resp. No severe side effects were seen, but presumably due to GM-CSF one patient developed an allergic type 1 reaction and one patient developed a possible pericardial exudation. Both were fully reversible after cessation of GM-CSF treatment.

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## THE PROGNOSTIC VALUE OF EPIDERMAL GROWTH FACTOR RECEPTORS, DETERMINED BOTH BY IMMUNOHISTOCHEMISTRY AND LIGAND BINDING ASSAY, IN PRIMARY EPITHELIAL OVARIAN CANCER (OC).

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Epidermal growth factor (EGF) can influence proliferation and differentiation of a wide variety of cells. In this study we investigated the presence and prognostic value of EGF-R with respect to progression-free survival (PFS) in 50 patients (pts) with primary OC. Median follow-up of the pts is 26 months, range 10-33 months. EGF-R was measured by one biochemical and 2 different immunohistochemical methods, in addition to oestradiol (ER) and progesterone (PgR) receptor. EGF-R by ligand binding assay and Scatchard analysis was detectable in 63% of the tumours, by immunohistochemistry with MoAb-2E9 in 82% and with MoAb-EGF-R1 in 78% of the tumours. ER-positivity was found in 58% and PgR-positivity in 38% of the pts. The results of measurements of EGF-R by the three different methods showed only weak to moderate associations with Spearman rank correlations (Rs) (Rs=0.13 and 0.45). ER and PgR were only weakly correlated (Rs=.20) and they showed no significant association with EGF-R status. There was no clear evidence of correlations between receptor values and FIGO stage or tumour rest. Univariate Cox regression analyses showed that higher FIGO stage and larger tumour rest were associated with shorter PFS (P=.001), while PgR positivity was associated with a longer PFS (P=.02). The level of EGF-R (irrespective of the method used) showed a positive correlation with the risk of progression, but this correlation was not statistically significant.

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## EVALUATION OF G-CSF ACTIVITY GIVEN BY INTRAMUSCOLAR (I.M.) ROUTE IN OVARIAN CANCER PATIENTS RECEIVING MITOXANTRONE (DHAD) + IFOSFAMIDE (IFO) AS SECOND-LINE (SL) THERAPY.

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Over recent years, G-CSF has been proposed in an attempt to increase the dose-intensity of chemotherapy (CT) and reduce the morbidity associated with CT given at standard doses. DHAD and IFO are cytotoxic agents with a well documented myelodepressive activity, in particular on neutrophils (NTR). Furthermore, the administration of both drugs concomitantly, at higher than conventional doses, in patients already treated with an intensive first-line treatment, is supposed to induce significant myelodepression. The aim of our study was to evaluate the myelotoxicity induced by the following SL regimen: DHAD 12 mg/m$^2$ i.v. days 1,21 and IFO 4 g/m$^2$ i.v. days 1,2,21. G-CSF was given i.m. at a dose of 5 mcg/kg/die on days 6-19. The regimen was given in an outpatient setting. 17 pts were treated for a total of 65 cycles. Median age was 44 (30-60). All pts received cis-platinum as first-line, 9 being treated at doses > 100 mg/m$^2$. 4/17 pts had been previously treated with SL treatments. Overall, mean time to NTR nadir was 8 days, with a mean duration of 5 days and a mean value of 200 mm$^3$. In 6/65 cycles no NTR nadir was observed. No evidence of cumulative toxicity for NTR or platelets was detected during the 5 planned CT cycles. Hematologic causes of treatment delays were registered in 5/65 cycles (4 due to anemia, 1 to neutropenia). 3 pts stopped chemotherapy for myelotoxicity (persisting neutropenia) and no toxic deaths were observed. Fever ($\geq$38°) was recorded in 15/65 cycles; 3 cases experienced an infective episode. Pts received antibiotics for 94 out of 1365 days of CT and RBC transfusions were given in 10/65 cycles. No bleeding episodes occurred. G-CSF was optimally tolerated, 2 pts referring grade 1 bone pain. In conclusion, G-CSF, given intramuscolar to ovarian cancer pts already treated with first-line CT, seems to be effective in reducing the neutropenia induced by our SL regimen. Further, randomized studies are needed.