parallel, controlled multicentre study evaluated the efficacy and safety of SC Epoetin alfa in reducing anaemia in MM pts refractory to conventional first or second line chemotherapy.

Epoetin alfa (150 IU/kg, 3 times/week initially, increased to a maximum dose of 300 IU/kg 3 times/week) was administered to 40 pts for 6 months. Thirty-one pts were entered into a non-treated control group. Chemotherapy continued during the study in both groups. A response was defined as the discontinuation of transfusion in transfusion-dependent pts (had received $\geq$2 transfusions in previous month) and an increase in Hb $\geq$ 2 g/dl in pts not transfusion-dependent. Overall, significantly more pts responded to treatment in the Epoetin alfa group (75% vs 21%, $P < 0.001$). In the 27 pre-transfused pts (11 controls, 16 Epoetin alfa) there was a trend towards reduced transfusional need in the Epoetin alfa group. In the 44 pts (20 controls, 24 Epoetin alfa) who were not pre-transfused, the mean Hb increase was significantly greater following Epoetin alfa treatment (+2.1 vs −0.2 g/dl, $P = 0.0001$). Increases in hematocrit and red blood cells were also significantly greater in Epoetin alfa-treated pts ($P = 0.0001$) and transfusion requirements were reduced (25% of Epoetin alfa-treated pts vs 45% of control pts). Epoetin alfa was well tolerated. In conclusion, in anaemic MM pts resistant to chemotherapy, Epoetin alfa is a well-tolerated treatment which significantly increases Hb levels in pts regardless of previous transfusions, and reduces transfusional needs in pts who have not received prior transfusions.

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CELL KINETICS OF HEMATOPOIETIC PROGENITORS FOLLOWING CHEMOTHERAPY (CT) PLUS COLONY-STIMULATING FACTORS (CSF'S) IN ADVANCED BREAST CANCER

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Appropriate timing of CSF's administration relative to CT is an important concern in trying to achieve the more effective myeloprotecion. Thirty patients with advanced breast cancer were treated with an intensified FEC regimen, planned at 21 days interval (5-FU 600 mg/sqm + Epirubicin 100 mg/sqm + CTX 750 mg/sqm, on day 1) sequenced with GM- (15 patients) or G-CSF (15 patients) both at 5 u/Kg/day, from day 3 to day 10. Using flow cytometry (FCM) we evaluated the proliferation kinetics of immunomagnetically selected CD34+ BM hematopoietic progenitors before CT and at different times after CSF's stopping. Both the sequence of FEC + GM- and FEC + G-CSF induced a rapid and sustained increase in both the percentage of BM myeloid precursors (BMMP%) and in the cycling status of CD34+ BM cells. However, while the BMMP% remained elevated in both cases after CSF's stopping, the enhanced proliferative activity of CD34+ cells decreased more rapidly after GM-CSF. The early administration of CSF's following CT increases the proliferative activity of CD34+ cells and makes myeloid BM hyperplastic, and this is effective in avoiding peripheral cytopenia. After CSF's stopping, the CD34+ cells proliferative activity subsided leading to a kinetic refractoriness of hemopoietic progenitors more evident after GM-CSF than following G-CSF. These data can be of value for a biologically drived optimal sequencing of CT and CSFs.

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PREVENTION OF ANAEMIA IN CANCER PATIENTS TREATED WITH CISPLATIN-CONTAINING CHEMOTHERAPY

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Cancer patients receiving cisplatin-containing chemotherapy frequently develop anaemia. This open-label, controlled multicentre study tested the safety and efficacy of Epoetin alfa treatment in the prevention of anaemia in patients (pts) with advanced cancer, receiving moderate-high doses of cisplatin (DDP)-containing chemotherapy. Three hundred pts with Hb levels $\geq$ 10 g/dl were randomized to receive either SC Epoetin alfa (150 IU/kg, 3 ×/week), starting on the first day of chemotherapy, and continuing for at least 12 weeks during at least 3 cycles of DDP, or no Epoetin alfa (control). One hundred and sixty-eight pts (82 in Epoetin alfa-treated group, 86 in control group) were fully evaluable (ie completed 3 cycles of DDP and had sufficient haematological data). The groups were divided into 4 sub-groups according to category of neoplasia; lung, ovary, head and neck, other. Baseline and demographic values were similar in both study groups.

The final Hb values were significantly higher in the Epoetin alfa-treated group (13.01 g/dl for Epoetin alfa group, 11.20 g/dl for control group; $P = 0.0001$) and in each of the four Epoetin alfa-treated sub-groups compared to the control sub-groups. Significantly fewer pts in the Epoetin alfa-treated group experienced the development or worsening of anaemia (final Hb < 10 g/dl) (9.8% of Epoetin Alfa-treated group vs 23.3% controls; $P = 0.02$). Six pts in each group received a red cell transfusion. Adverse effects were detected in 8.3% of the Epoetin alfa-treated group, approximately half attributable to Epoetin alfa.

In conclusion, Epoetin alfa 150 IU/kg (administered 3 ×/week) safely maintained Hb levels and significantly reduced the incidence of anaemia in patients with neoplasias, regardless of tumour type.

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IMMUNOHISTOCHEMICAL EVIDENCE OF CYTOPLASMIC AND INTERSTITIAL TRANSFORMING GROWTH FACTOR β3 (TGF β) IN MYELOPROLIFERATIVE DISEASES (MPD)

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TGFβ is known to be involved in the pathogenesis of idiopathic pulmonary fibrosis and liver fibrosis, which is reversible after anti-TGFβ therapy. In bone marrow biopsies (bmb) an increased number of TGFβ positive sinus in M3 leukemia is known (Raza 93). We were interested to look for a correlation of TGFβ positive interstitial structures and b.m. fibrosis. Bmb were dissolved in histocon and frozen with butan methanol in N2. In indirect immuno-alkaline-phosphatase TGFβ and CD61 were stained with mo-ab supplied by Oncogene and Dakopatts. We performed a quantitative evaluation of TGFβ and CD 61 positive cells and a qualitative examination of TGFβ positive interstitial structures according to density in a score of 0–5 similarly to Raza.

Bmb of 10 patients (pts) with MPD at the Hannover classification were evaluated: CML 4 pts (CT No 1, 3; MI No 2, 4); Megakaryoblastic 2 pts (No 5, 6); PTH 1 pt (No 7): MFS 1 pt (No 8 by CMGM): OMS 2 pts (No 9, 10). Fibrosis was strong (grade III) in pts No 8 to 10, minimal (grade I) in pts No 2 and 5 and none in all other pts. The number of CD 61 positive megakaryocytes was higher than the number of TGFβ positive cells in all cases (41.3 vs 28.1 cells/mm^2). TGFβ was strongly increased (Score 4, 5) in pts with a high number of immature megakaryocytes (No 5, 6), and minimal or none fibrosis was seen. TGFβ was moderate (score 3) in MFS (No 8) and minimal or none in all other pts. *In conclusion:* no correlation exists between the degree of fibrosis and TGFβ, and the highest expression of TGFβ was shown in cases with high content of immature megakaryocytes and none or minimal fibrosis.

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A MULTI-INSTITUTIONAL RANDOMISED STUDY ON THE EFFECTIVE SCHEDULE OF LENOGRASTIM ADMINISTRATION IN PEDIATRIC CANCER PATIENTS

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[Objective] A multi-institutional randomised study was performed to compare 1-hour and 24-hour intravenous drip infusion in order to determine the effective schedule of lenograstim (rhG-CSF) for treatment of neutropenia associated with chemotherapy of malignant tumours in paediatric patients. *[Subjects and Methods]* Paediatric patients with lymphoid tumours who are supposed to receive high dose Ara-C were divided into two groups, 1-hour and 24-hour intravenous drip infusion of rhG-CSF 5 μg/kg on post-chemotherapy day 1. Solid tumour patients receiving A1 or new A1 protocol of chemotherapy were divided into 4 groups, 1-hour and 24-hour intravenous drip infusion of rhG-CSF on day 1 or day 4, respective. *[Results and Discussion]* Comparison of 24-hour and 1-hour intravenous drip infusion of rhG-CSF showed that the recovery of neutrophils was quicker and the duration of rhG-CSF administration was shorter in 24-hour continuous intravenous administration. In patients with solid tumour, the nadir value of neutrophil count was higher and the duration of neutrophil count less than 200/μl was shorter in day 1 group when compared with day 4 group. These data suggest that continuous and earlier administration of rhG-CSF is more effective in our setting.