Results:

	A (n = 25)	B (n = 13)	Mann-Whitney p value
Total cell count ($\times 10^8$)	6.6 (4.05–12.18)	4.06 (30–7.72)	0.0002
CFU-GM ($\times 10^4$/kg)	3.14 (0.44–24.5)	3.35 (0.06–21.27)	NS
CD34+ ($\times 10^6$)	43.6 (0.3–337.7)	38.5 (4.1–1187.7)	NS
Days to engraftment	12 (6–21)	12 (8–23)	NS

Conclusions: Although Regimen A led to increased mononuclear cell count there was no difference in the CFU-GM or CD34+ counts or days to engraftment. Reduction of stem cell harvest time from 4 to 2 days has economic benefits and improves patient tolerability.

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A PHASE III TRIAL OF RECOMBINANT GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR (GM-CSF) AS CORRECTIVE TREATMENT IN PATIENTS (PTS) WITH NEUTROPENIC FEVER FOLLOWING ANTINEOPLASTIC CHEMOTHERAPY (CT): RESULTS OF AN INTERMEDIATE ANALYSIS

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Fifty-one patients (pts) with neutropenic fever (fever $\geqslant 38.5°$ C at 3 hour-interval and an absolute neutrophil count (ANC) $< 1.10^9$/l) following chemotherapy have been included. All had a non-myeloid tumor and an ECOG performance status $\leqslant 2$ at the beginning of the last CT course. None had received G or GM-CSF as prophylactic treatment nor prophylactic antibiotherapy or glucosteroids during the last 10 days.

Patients were hospitalized and randomized, in the 12 hours following the beginning of fever, to receive either IV antibiotherapy (control group) or antibiotherapy and GM-CSF, given subcutaneously at a daily dose of 5 μg/kg, to be continued until 2 days after the recovery of ANC $\geqslant 1.10^9$/l. A stratification was done, before randomization, according to chemotherapy level of hematologic toxicity [i.e.: high (HCT) versus moderate (MCT)]. There were 19 male and 32 female, with a median age of 50.8 years old (18–79). Twenty-five pts had received HCT and 26 MCT. Results are summarized in the table below:

Treatment arm	**GM-CSF**	**Control group**	**Wilcoxon's test (p)**
number of pts	26	25	
median days with ANC $< 0.5\times10^9$/l (range)	3 (1–8)	4 (1–9)	0.06
median days with ANC $< 1\times10^9$/l (range)	3 (1–10)	6 (2–12)	<0.001
median days with ANC $< 0.5\times10^9$/l, HCT pts (range)	3 (1–18)	4 (1–6)	0.66
median days with ANC $< 1\times10^9$/l, HCT pts (range)	4 (1–10)	5 (2–12)	0.22
median days with ANC $< 0.5\times10^9$/l, MCT pts (range)	2 (1–4)	4 (1–9)	0.04
median days with ANC $< 1\times10^9$/l, MCT pts (range)	3 (1–5)	7 (2–10)	<0.001
median days with fever $\geqslant 38.5°$	2.5 (1–7)	2 (1–12)	0.39

One pt, in the control group, died with infection. Side effects related to GM-CSF consisted in mild bone pain in 2 pts. In conclusion, GM-CSF, given as corrective treatment, significantly reduced the duration of neutropenia (days with ANC $< 1\times10^9$/l) following chemotherapy. At time of analysis, this effect appeared more pronounced after moderately hematotoxic chemotherapy rather than after highly hematotoxic chemotherapy. These results will be updated for presentation.

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GROWTH FACTORS IN COMBINATION: PHASE I STUDY OF DOSE INTENSIFIED CARBOPLATIN (CB), CYCLOPHOSPHAMIDE (CT) AND ETOPOSIDE (VP) IN PATIENTS (PTS) WITH ADVANCED, REFRACTORY CANCER

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This phase I study was designed in order to verify the toxicity of CB. CTX, VP given at high doses, in combination with GCSF alone or GCS and GMCSF given sequentially. The two lymphokines, with different properties, might have their ideal integration in the sequential administration. A group of 10 heavily pretread patients (PTS) with stage IV disease (2 breast cancer, 2 small cell and 1 non small cell lung cancer, 1 sarcoma, 1 colorectal cancer, 1 ependymoblastoma, 1 signet-ring cell bladder cancer, 1 neuroendocrine prostate cancer) were enrolled into the study between August and September 1994. Median (M) PS (ECOG) was 1, M age 41 years (22–65). Previous treatments: 7 PTS had surgery, 4 PTS had radiotherapy, all PTS had received previously a median of 4.5 chemotherapy courses (4–12). CB-CTX-VP combination was administered over 3 days. Each patient, received two courses of the same CT, followed, randomly, either by 14 days of GCSF (arm A) or by 7 days of GCSF and 7 days of GMCSF (arm B) with cross over in the second CT course. Both growth factors were given sq at the dose of 5 μg/kg/day. CB dose was calculated according to Calvert *et al.* (*JCO* 1989, **7:1748**) and expressed with the area under the concentration versus time curve (AUC). All patients received an outpatient treatment. The maximum tolerated doses of CTX and VP, found in a previous work (*Ann Oncol* 1994, **5:90,**), were, respectively, 1500 and 400 mg/m^2, while CB doses ranged from 5 to 8 AUC. Twenty chemotherapy courses over 20 are evaluable. Absolute neutrophil count (ANC) < 1000 μL for 54 days in arm A versus 68 days in arm B ($P = 0.02$); platelets (PLT) count $<$ 25.000 μL: 57 days arm A versus 30 days in arm B ($P = 0.03$); days of hospitalisation 35 in arm A versus 16 in arm B ($P = 0.75$); platelets transfusion: 107 Vs 58 ($P = 0.02$); PRBCS 15 vs 5 ($P = 0.25$). No treatment related death occurred. At the present time, eight patients had responses and are alive. These data indicate that dose intensified CT may be delivered safely; GCSF alone shortens days of neutropenia, the combination of the 2 cytokines shortens the time of thrombocytopenia and decreases the number of platelets transfusions.

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EVALUATION OF THE EFFICACY OF G-CSF IN NEUTROPENIA INDUCED BY RT ALONE OR COMBINED WITH IMMUNOTHERAPY

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Extensive field irradiation of the pelvis induces neutropenia. The combination of RT with interferon results in a lower absolute neutrophil count. Thirty patients (pts) with stage III cancer of the uterine cervix were treated either with exclusive RT (group A, 10 pts) or with RT and 3.000.000 iu/d interferon plus isoretinoin 30 mg/d (group B, 20 pts). The immunotherapy duration was 2 months. The total RT dose in both groups was 54 Gy external beam RT and 20 Gy intracavitary Brachytherapy. The absolute neutrophil count of the beginning of the treatment did not exceed 4×10^8 I. G-CSF was administered only on days when the absolute neutrophil count was less then 2×10^9 I. G-CSF was not used prophylactically but upon indication. Neutropenia was corrected in all cases. Patients undergoing RT received at least 4 injections and the ones with the combined modality treatment 6–8 injections during the overall treatment time. The correction of the absolute neutrophil count allowed the continuation of treatment without interruptions that influence the local control. The efficacy of the G-CSF administration was immediately detectable. The neutrophil count rose to $5–6 \times 10^9$ I, on the following day, thus being promptly corrected. No adverse effects of G-CSF were observed. These results show the efficacy of G-CSF that can be used upon indication and not prophylactically.