health status was assessed at baseline and after 6 and 12 weeks of treatment via a self-administered questionnaire combining validated psychometric scales, including energy, physical/social/cognitive role function and mental health. The two groups were comparable in baseline clinical, demographic and health status measures. Treatment with Epoetin alfa was well tolerated. The baseline Hct was 27.5 in the Epoetin alfa group, and 27.7 in the pbo group. The mean final Hct increased by 5.7 percentage points in the Epoetin alfa-treated group, and by 1.5 percentage points in the pbo group ($P < 0.0001$). Approximately 50% of the Epoetin alfa group had a Hct change of ≥ 6 points over baseline values unrelated to transfusion vs approx 15% of the pbo group ($P < 0.0001$). Overall, about 30% of the Epoetin alfa-treated pts achieved a Hct ≥ 38, unrelated to transfusion, vs approx 5% in the pbo group ($P < 0.0001$). For all pts, between group differences favouring the Epoetin alfa group were found for energy scores ($P < 0.05$). In addition, Epoetin alfa-treated pts whose Hct reached 38% showed significant improvements in energy, self-rated health, physical function, role function/physical, role function/emotional, social function, and mental health ($P < 0.01$ to $P < 0.0004$) vs pbo pts. The results show that Epoetin alfa improves Hct in anaemic CLL pts, and the impact of Epoetin alfa treatment on health status is greatest in pts showing a substantial Hct response.

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A PHASE IV STUDY OF EPOETIN ALFA EXAMINING CLINICAL OUTCOMES IN ANAEMIC CANCER PATIENTS RECEIVING CHEMOTHERAPY

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This Phase IV study, involving over 570 U.S. community-based oncology practices, aimed to measure clinically relevant outcomes in 2,030 Epoetin alfa-treated anemic patients (pts) with solid or hematological tumors, who were receiving chemotherapy. Patients received Epoetin alfa 150 IU/kg 3 times weekly for up to 4 months. If necessary, this dose could be increased to 300 IU/kg 3 times weekly after 8 weeks of therapy. Quality of life (QOL), mean change in hemoglobin (Hb) level and avoidance of transfusion were assessed. One thousand, four hundred and ninety-eight pts had both baseline and end values. The mean changes in energy level, activity level, and overall QOL from baseline were increased significantly (+38%, +32%, +24%, respectively; $P < 0.001$). These improvements correlated directly with a significant increase in Hb level from baseline (+1.7 g/dl; $P < 0.001$, $r = 0.254$). In the month before therapy, 22% of pts were transfused. During months 2, 3 and 4, the percentage steadily decreased (15%, 11%, 10%; $P < 0.001$ compared to baseline). Fifty-nine percent of pts were transfusion-independent after month 1. Forty-one percent of pts discontinued therapy—22% because of illness, adverse effects, or death (none drug related), 19% because of disease progression, discontinued chemotherapy, or personal reasons. In conclusion, the Epoetin alfa-treated anaemia cancer pts assessed experienced significantly improved QOL. Transfusion requirements were significantly reduced, and Hb levels increased significantly. Epoetin alfa was well tolerated.

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REDUCTION OF THE RISK OF TRANSFUSION IN PATIENTS WITH SMALL CELL LUNG CANCER (SCLC) UNDERGOING CHEMOTHERAPY

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This open-label, controlled, multicentre study examined the efficacy of subcutaneous (SC) Epoetin alfa (administered 3 times weekly) in preventing anaemia in 130 initially non-anaemic (Hb $\geq$ 10.5 g/dl) SCLC patients (pts) scheduled to receive 4–6 cycles of platinum-based combination chemotherapy.

Patients were randomized to receive Epoetin alfa 300 IU/kg (group A, n = 44), 150 IU/kg (group B, n = 42) or no Epoetin alfa (group C). Treatment began 1 day after completion of the monthly chemotherapy cycle, and finished 3 days before initiation of the next cycle, for up to 6 cycles. Reductions in Epoetin alfa dose were made if Hb $\geq$ 15 g/dl. Logistic regression analysis of group C pts showed that low baseline Hb levels or a reduction in Hb level from higher baseline Hb levels, during the first cycle of chemotherapy, were important risk factors for transfusion. Group C required significantly more transfusions than Groups A and B (59%, 21%, 45%, respectively; $P \leq 0.05$). In addition, significantly more pts in group C experienced reduced Hb levels (Hb < 10 g/dl) than those in Groups A and B during cycles 2–5 (66%, 48%, 39%, respectively; $P \leq 0.05$). Epoetin alfa was well tolerated.

In conclusion, Epoetin alfa is effective and well tolerated in preventing anaemia and reducing the risk of transfusion in SCLC pts undergoing cyclic chemotherapy.

235 POSTER

COMPARISON OF TWO STRATEGIES FOR THE TREATMENT OF RADIOGENIC LEUKOPENIA USING G-CSF

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Background: Iatrogenic leukopenia can cause radiotherapy to be delayed or discontinued. This complication can be overcome with the use of granulocyte colony-stimulating factor (G-CSF). However, great uncertainty exists regarding the mode of application of G-CSF in patients treated with radiotherapy. For this reason, the efficacy of two strategies for the administration of G-CSF in irradiated patients was compared in a prospective randomized clinical study. *Material and Methods:* Forty-one patients who developed leukopenia whilst undergoing radiotherapy were treated with G-CSF at a daily dose of 5 μg per kg.. The first group received single injections of G-CSF as and when required (n = 21). The second group received G-CSF on at least 3 consecutive days (n = 20). *Results:* An increase in leucocyte values in the peripheral blood was observed in all patients treated with G-CSF. In the group which received G-CSF when required, two injections (range: 1–8) were administered in most cases. In the second group, most of the patients received 3 injections (range: 3–9). The average duration of therapy interruptions was 4.8 days (0–28) in the first therapy arm and 2.5 (0–20) in the second arm. The variance in the duration of therapy interruptions between the 2 groups was not significant ($P = 0.2$). Radiotherapy had to be terminated in 2 patients due to thrombocytopenia. *Conclusion:* Our results reveal that G-CSF is effective in the treatment of radiogenic leukopenia regardless of the mode of application. The administration of G-CSF on several consecutive days tends to reduce the number of therapy interruptions more effectively than single injections given when required.

236 POSTER

MAP KINASE REGULATION BY PHOSPHATASE 2A IN RESPONSE TO EGF IN A431 CELLS

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EGF is involved in the regulation of cell proliferation in normal as well as in neoplastic tissues. The A431 cells display *in vitro* ambivalent growth properties in response to EGF. We recently demonstrated that the dual effect of EGF is associated to differential mechanisms of p42 MAP Kinase regulation since stimulatory doses of EGF leads to a moderate but persistent activation of MAP Kinase, whereas an abrupt but transitory activation is induced by inhibitory EGF concentrations. In order to clarify the mechanism of MAP Kinase regulation under conditions of positive and negative growth regulation, we have measured the activity of Phosphatase 2A. Our data demonstrate an inverse correlation between PP2A and MAP Kinase activities. Moreover, the addition of 2 nM okadaic acid in A431 cell cultures treated with inhibitory concentrations of EGF inhibits the PP2A activation while restoring MAP Kinase activity.

In conclusion, our data suggest that the activation of MAP Kinase by EGF in A431 cells probably involves the inhibition of PP2A, resulting in an increase of available phosphorylated MAP Kinase

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THE EFFECTIVENESS AND TOLERABILITY OF RECOMBINANT HUMAN ERYTHROPOIETIN (EPOETIN ALFA) IN PATIENTS WITH MULTIPLE MYELOMA REFRACTORY TO CHEMOTHERAPY

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Anaemia is common in patients (pts) with multiple myeloma (MM), and becomes chronic in pts resistant to chemotherapy. This randomized,