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# Increasing the Dose Intensity of Chemotherapy by Means of Granulocyte-colony Stimulating Factor (G-CSF) Support in the Treatment of Small Cell Lung Cancer (SCLC)

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We were interested to read that Gruppo Oncologico Centro-Sud-Isole (GOCSI), by using granulocyte-colony stimulating factor (G-CSF) support, successfully increased the dose intensity of carboplatin, epirubicin and etoposide (CEV) in the treatment of SCLC by giving high doses of epirubicin and etoposide and by reducing the interval between cycles from 4 to 3 weeks [1]. Their study provides important confirmatory evidence of the feasibility of this policy to that reported from a pair of parallel phase II studies conducted by the MRC Lung Cancer Working Party [2, 3]. We were able to give ACE chemotherapy (doxorubicin, cyclophosphamide, etoposide) at intervals of only 2 weeks, instead of the usual 3 or 4 weeks, by giving either glycosylated [2] or methionyl [3] recombinant human G-CSF daily between the chemotherapy cycles. We should like to make two comments arising from these MRC and GOCSI reports.

First, we, like they, reported substantial levels of toxicity. We feel that these levels are acceptable when dose intensification is being used in an attempt to improve long-term survival in patients with relatively good prognosis. We included in our studies patients with limited or extensive disease, but they had to have good performance status (WHO grade 0–2) [4]. GOCSI restricted their intake to patients with extensive disease, albeit with good performance status, but do not give their reasons for this.

Secondly, GOCSI imply that this dose intensification policy is unlikely to prove beneficial. They do so on the basis that toxicity was severe, that the response rates were similar to those reported previously with conventionally scheduled CEV chemotherapy, and that reports in the literature show that novel weekly regimens did not improve survival compared with standard regimens in randomised trials [5, 6].

In our opinion, they are being prematurely pessimistic. No reliable comparisons between weekly and conventionally scheduled regimens with respect to dose intensity and outcome can be made. In both the trials they cite, received dose intensity was substantially lower with the weekly than with the standard regimens and the drugs in the two regimens were different; the only randomised comparison that will establish the value or otherwise of dose intensification is one comparing an accelerated regimen versus the same drugs given conventionally [7]. Indeed, the main justification for the sort of phase II studies discussed is to assess the feasibility and acceptability of the dose intensification policy before proceeding to a randomised trial comparing the same regimen given at either increased or conventional dose intensity. The MRC Lung Cancer Working Party adopted precisely this approach. With support from Chugai-Rhône-Poulenc, we are now conducting a randomised trial (LU19) comparing ACE plus G-CSF given every 2 weeks versus ACE given every 3 weeks. In both groups, dose delay but not dose reduction is recommended in the management of toxicity. The planned intake of 400 patients has just been completed. The primary endpoint is survival, but we are also studying some important secondary endpoints, including interval between cycles of chemotherapy, myelotoxicity, quality of life and days in hospital.

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