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Increased Blood Cell Destruction During Vigorous Regeneration of Bone Marrow after Intensive Chemotherapy for Non-Hodgkin Lymphoma

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WE HAVE reported a new high dose regimen for the treatment of non-Hodgkin lymphoma (NHL), CAMBO-VIP[1], consisting of four myelosuppressive drugs (doxorubicin, cyclophosphamide, etoposide and ifosfamide) and four non-myelosuppressive drugs (vincristine, methotrexate with leucovorin rescue, bleomycin, and prednisolone), administered during alternate weeks for a total period of 12 weeks. We obtained a high response rate and prolonged disease-free survival with this regimen. The treatment was well tolerated: myelosuppression was severe but transient and caused no serious infectious complications.

However, we noticed transient elevation of serum lactate dehydrgenase (LDH) level in some patients at or shortly after the completion of CAMBO-VIP treatment. 18 of 36 patients who were treated with this regimen showed LDH level over 1.5 times normal values, and 6 of them displayed over 3-fold normal values. LDH elevation was not associated with liver function abnormality as demonstrated by elevation of transaminases or total bilirubin. All of these patients were in complete or partial response with no evidence of tumour progression. Therefore, some other factors must be considered as the cause of LDH elevation. Klimo *et al.*[2] reported similar elevation of serum LDH of unknown aetiology after completion of MACOP-B treatment for NHL. Elevation of serum LDH in our patients consisted of increase in isozymes LDH_1 and LDH_2. Interestingly, serum haptoglobin was undetectable in all 6 patients who were examined at the time of LDH elevation. Reticulocytosis and leukoerythroblastosis in peripheral blood were also observed in all of these 6 and other patients. In one particular patient, as many as 166 erythroblasts per 100 white blood cells were counted. These abnormalities, including LDH elevation, returned to normal relatively rapidly, usually within 2–3 weeks.

These abnormalities suggest transient excessive blood cell destruction which might be associated with vigorous recovery of haemopoiesis following chemotherapy-induced myelosuppression. Haemopoiesis may become temporarily defective as a result of rapid cell proliferation, to such an extent that a proportion of newly formed cells are prematurely destroyed in the bone marrow or soon after they appear in the peripheral blood. Granulocyte or granulocyte–macrophage colony stimulating factors may augment these abnormalities, when they are used to expedite the recovery of bone marrow function following chemotherapy-induced suppression.

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Erythropoietin Treatment of Anaemia Associated with Lymphoproliferative Disorders

Stefano Molica

A DECREASED ERYTHROPOIETIN (EPO) response to anaemia has been reported in cancer patients and in those receiving cytotoxic chemotherapy [1]. This finding suggests that anaemia in cancer patients is, at least partially, due to a relative deficiency of EPO and that therapy of anaemia with recombinant human EPO (rHuEPO) may be appropriate in such patients [2–4].

To investigate this a prospective phase II study of rHuEPO has been carried out in 11 patients with haemoglobin levels < 9 g/dl (median 7.5 g/dl; range 6.7–8.8) who were being followed-up for lymphoproliferative disorders. The patient cohort included 3 chronic lymphocytic leukaemia (CLL) and 8 multiple myloma (MM) cases. There were eight males and three females. The average age was 63.3 years (S.D. 11). Clinical and haematological details are summarised in Table 1.

rHuEPO (Eprex, Cilag) was administered three times a week by subcutaneous route on an outpatient basis at an initial dose of 50 U/kg body weight. The aim of treatment was a haemoglobin level of 10 g/dl without transfusion and this was defined as a complete response (CR). If CR was not achieved within 4 weeks, the rHuEPO dose was increased to 75,100 and 150 U/kg body weight at 4-week intervals. If there was no response within 16 weeks, rHuEPO treatment was discontinued.

rHuEPO was given simultaneously to alpha interferon in 2 MM patients. All CLL patients were receiving concomitant therapy with an alkylating agent (chlorambucil or cyclophosphamide) associated with low doses of steroids. For the remaining 6 MM patients treatment consisted of alternating courses of alkeran plus prednisone in 4 cases, cyclophosphamide plus high doses of dexametasone in 1 patient, and polychemotherapic regimen (DAV/CD/CED) in 1, respectively.

7 out of 11 patients (5 MM, 2 CLL) responded to rHuEPO therapy maintaining haemoglobin levels above 10 g/dl without transfusions. The median dose of rHuEPO requiring anaemia correction was 75 U/kg body weight (range 50–100). In responding MM patients, no correlation was found between the amount of serum M component and the simultaneous determination of haemoglobin levels ($r = -0.10$). This supports

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