Improvement in quality of life for cancer patients treated with epoetin alfa

S.E. LIBRETTO, PHD BSC MIBIOL CBIOL, *Janssen-Cilag Ltd, High Wycombe, Buckinghamshire,* P.J. BARRETT-LEE, MD BSC FRCP FRCR, *Clinical Trials Unit, Velindre Hospital, Cardiff, Wales*, K. BRANSON, BA MB BCHIR MRCP, *Adult Leukaemia Unit, Christie Hospital, South Manchester,* D.W. GORST, BM BCH MA FRCP FRCPATH, *Department of Haematology, Royal Lancaster Infirmary, Lancaster,* R. KACZMARSKI, MD MRCP MRCPATH, *Department of Haematology Medicine, Hillingdon Hospital, Uxbridge, Middlesex,* K. McADAM, MRCP, *Haematology and Oncology, Peterborough District Hospital, Peterborough,* P. STEVENSON, RGN, *Cancer Centre, Newcastle General Hospital, Newcastle upon Tyne* & R. THOMAS, MRCP MD FRCP, *Primrose Unit, Bedford Hospital, South Wing, Bedford, Bedfordshire, UK*

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Anaemia is a common complication of cancer and cancer therapies, and fatigue is one of the most common symptoms of anaemia, disrupting functional performance and reducing overall quality of life. The positive effects of treating renal patients with recombinant human erythropoietin are well documented. This case report series details the specific effects of fatigue on individual patients with cancer and their way of life, and describes their significant improvement in lifestyle following the reversal of anaemia using recombinant human erythropoietin, epoetin alfa.

Keywords: human erythropoietin, epoetin alfa, quality of life.

INTRODUCTION

Anaemia is characterized by fatigue, vertigo, headache, shortness of breath, chest pain, weakness and decreased motivation (Cella 1998). It is a common complication in cancer and cancer therapies and can be the result of aggressive disease or aggressive therapy (Cella 1998).

The aetiology of anaemia is probably multifactorial, and includes factors such as aberrant ferrokinetics associated with chronic disease, poor nutritional status, bleeding and bone marrow infiltration with tumour (Spivak 1994). Levels of endogenous erythropoietin, which stimulates the production of red blood cells, are significantly lower in anaemic patients with cancer than in patients with a similar degree of anaemia caused by iron deficiency (Dainiak *et al*. 1983; Miller *et al*. 1990). The development and persistence of anaemia in cancer patients may therefore be the result of a blunted erythropoietin response to anaemia. Chemotherapy leads to a significant fall in haemoglobin concentration (Hb) across all cancer diagnoses (Ludwig & Fritz 1998) and its administration to patients with cancer may consequently exacerbate both anaemia and the relative erythropoetin deficiency.

The incidence of anaemia in patients with cancer varies according to tumour type, the prescribed chemotherapeutic agents and the number of chemotherapy cycles administered (Barrett-Lee *et al*. 2000). In a large-scale audit of 2719 patients in the UK, the mean proportion of patients with a Hb of less than 11 g/dL rose from 17% during the first cycle of chemotherapy to 38% by the sixth cycle, despite transfusion in 33% of patients (Barrett-Lee *et al*. 2000). In addition, the proportion of patients receiving

Correspondence address: Dr S. E. Libretto, Janssen-Cilag Ltd., PO Box 79, Saunderton, High Wycombe, Buckinghamshire HP14 4HJ, UK (e-mail: slibrett@jacgb.jnj.com).

transfusions increased markedly if the pretreatment Hb was below 10 g/dL.

In clinical practice, transfusions for anaemia were required by 18% of all patients with solid tumours and those with lung cancer had the highest rate (34%) (Skillings *et al*. 1993). Of those with the haematological malignancies, leukaemia and lymphoma, 78% and 25% were transfused with red cells because of anaemia respectively. Anaemia is present at diagnosis in almost 70% of patients with multiple myeloma and can be severe (Dalton 1998). However, in a large-scale audit that included patients with cancer of the lung, ovaries or breast (n = 2506), the incidence of anaemia assessed indirectly by the requirement for blood transfusion was 43%, 41% and 19%, respectively, and the proportion of these patients requiring more than one transfusion was 22%, 21% and 7% respectively (Barrett-Lee *et al*. 2000).

Fatigue is one of the most common symptoms of anaemia, occurring in 61–96% of patients with cancer undergoing chemotherapy (Irvine *et al*. 1991, 1994). Anaemia-related fatigue can disrupt functional performance and reduce overall quality of life (QoL) (Irvine *et al*. 1994). According to a recent survey designed to assess the emotional, social, physical and economic impact of fatigue after chemotherapy in 379 cancer patients, 76% experienced fatigue at least once a week, 91% of whom reported that it prevented them from leading a 'normal' life (Curt *et al*. 1999). Three-quarters (133) of those employed (177) were forced to reduce their work hours or stop altogether, and 20% of caregivers took leave from or reduced their responsibilities at work. In spite of this, over half of patients with cancer have never reported this symptom to the hospital doctor and only one-seventh have received treatment or advice about fatigue management (Stone *et al*. 2000).

Blood transfusion is currently the most common form of treatment of patients with anaemia. However, the proportion of anaemic patients increases with repeated cycles of chemotherapy despite blood transfusions, suggesting that the benefit of transfusion is only short lived (Barrett-Lee *et al*. 2000).

Anaemia can also be treated with erythropoietin, a hormone produced by the kidney that stimulates the production of red blood cells. Several clinical trials have studied the effects of epoetin alfa administration to anaemic patients with cancer receiving myelosuppressive chemotherapy. Effects on non-cisplatin and cisplatin chemotherapy have been considered separately because of the potential for cisplatin to cause renal impairment (Bray & Reaman 1991). Trials have demonstrated the efficacy of epoetin alfa in both treatment groups in increasing Hb, energy levels and ability to perform daily activities, raising overall QoL and reducing blood transfusion requirements (Platanias *et al*. 1991; Miller *et al*. 1992; Abels 1993; Cascinu *et al*. 1993, 1994; Case *et al*. 1993; Henry & Abels 1994, 1995; Littlewood *et al*. 1999). Results of controlled clinical trials have been confirmed in two large community-based studies of epoetin alfa in anaemic patients with cancer receiving chemotherapy (Glaspy *et al*. 1997; Demetri *et al*. 1998).

Clinical trials provide information on the overall effects of a treatment on a patient population but usually do not detail the specific effects on the individual and their way of life. The following case reports describe the improvement in lifestyle of patients with solid and haematological cancers whose treatment included the administration of recombinant human erythropoietin [Epoetin alfa (Eprex®), Janssen-Cilag Ltd]. The cases show how increasing Hb and reversing anaemia revokes fatigue and improves the QoL of a patient.

In addition, the opportunity has been taken to include some case reports of patients involved in clinical trials that have used established validated questionnaires to determine the effect of epoetin alfa on QoL.

CASE REPORTS OF SOLID TUMOURS

Lung cancer

Case 1

Mrs R., who had not smoked for 20 years, was 68 years of age when she was referred to hospital following several weeks of productive cough with haemoptysis that showed no sign of abating. A chest radiograph revealed a large mass in the left lung and the results of a subsequent biopsy confirmed the mass to be squamous cell lung carcinoma. On presentation, her main symptoms were an irritating cough with intermittent haemoptysis, hoarseness of voice and dyspnoea. She was pale and reported that, despite these symptoms, she managed to soldier on.

Regardless of four courses of mitomycin–ifosphamide–cisplatin and dexamethasone, disease progression occurred 4 months later and a decision was made to administer six cycles of carboplatin. Blood tests showed that Mrs R.'s Hb was 12.0 g/dL before the first cycle of carboplatin but, within 4 weeks of receiving chemotherapy, had fallen to 10.0 g/dL.

Mrs R. consented to participate in a clinical trial and was randomized to receive 10 000 units of epoetin alfa three times per week for 4 months. Epoetin alfa therapy commenced after the second course of carboplatin when

her Hb was 9.0 g/dL. After 4 weeks her Hb had risen to 10.3 g/dL and by the eighth week was 11.0 g/dL. The increase continued over the next 11 weeks to 13.3 g/dL, at which time epoetin alfa therapy was stopped.

Mrs R. felt well throughout her epoetin alfa therapy and only reported occasional episodes of mild fatigue. Her breathlessness and cough disappeared and the improvement encouraged her to take a holiday in Tenerife about 6 weeks after starting epoetin alfa and another in Malta 3 months later. Blood tests taken 4 months after the end of epoetin alfa therapy showed her Hb had stabilized around 10 g/dL.

Unfortunately, Mrs R.'s condition deteriorated over the following 6 months and she subsequently died in hospital.

Ovarian cancer

Case 1

Mrs P. is 69 years of age and has Stage III ovarian carcinoma. She received six cycles of carboplatin and experienced severe fatigue after the first cycle. On presentation she was very pale and reported feeling very lethargic and dozing off if she sat down. Her husband and grown-up son were very supportive and accompanied her each time she attended hospital, but were clearly concerned about her condition. They reported that she had no energy and sat in her chair all day and her husband had taken over many domestic tasks.

Blood tests showed that her Hb had fallen from 12.0 to 9.3 g/dL within the first 4 weeks of chemotherapy. She consented to enter a clinical trial and was randomized to receive 10 000 units of epoetin alfa three times per week for 4 weeks. After 2 weeks of epoetin alfa therapy, Mrs P.'s Hb had risen to 11.1 g/dL and her reticulocyte count had increased from 38 to 84 $\times$ 10^9/L. By the fourth week her Hb was 13.7 g/dL and reticulocytes were 188 $\times$ 10^9/L, so the epoetin alfa was stopped for 1 month until her Hb had fallen to 10.7 g/dL. It was restarted at a dose of 7500 units thrice weekly and Mrs P remained free from anaemia during the rest of her course of carboplatin.

She then underwent an elective total hysterectomy and debulking surgery, and required no blood transfusions before or during surgery. Surgery was followed by two cycles of cisplatin and cyclophosphamide.

Treatment of Mrs P.'s anaemia affected the QoL of herself and her family. She was no longer lethargic and was able to resume some of her normal activities. She regained interest in socializing with her family and close friends that she had previously felt too tired to enjoy. Her ability to perform household tasks was important for her self-esteem and relieved her husband of extra work. Both Mrs P. and her family were able to have a more positive outlook on her disease.

Case 2

Mrs M. is 58 years of age. On presentation she was pale with a distended, bruised abdomen and a swollen left ankle with pitted oedema. Chest auscultation revealed right pleural effusion and ultrasound delineated a 12 cm pelvic mass with right hydronephrosis and ascites. Laparotomy showed metastatic tumour deposits throughout the abdomen, although omenectomy did not permit any degree of debulking. The pathology report confirmed that she had inoperable Stage IV ovarian carcinoma involving the pleura and that her case was complicated by deep vein thrombosis.

This lady was prescribed a course of six four-weekly cycles of carboplatin. She showed some clinical improvement after the first 5 weeks of chemotherapy, although blood tests showed that her Hb had fallen from a pretreatment value of 9.9–7.5 g/dL. She reported increasing tiredness and that she 'felt anaemic'.

Mrs M. consented to participate in a clinical trial and was randomized to receive epoetin alfa therapy, 10 000 units three times a week for 3 months. About 2 weeks after her first dose of epoetin alfa and fourth cycle of carboplatin, her Hb was still low (6.6 g/dL). As she was also neutropenic and thrombocytopenic the decision was made to transfuse her with three units of blood.

After 5 weeks of epoetin alfa therapy, Mrs M.'s Hb had risen to 12.4 g/dL. After 6 weeks the dose was increased to 20 000 units three times per week. Subsequently, her Hb was maintained between 11.2 and 13.5 g/dL until the end of the epoetin alfa treatment period, i.e. 1 month after the last cycle of carboplatin. At this stage, she looked remarkably well. She was no longer tired, lethargic and generally washed out but was able to undertake more daily activities.

One month later, Mrs M. underwent debulking surgery and the histology report confirmed malignant disease in the ovaries, uterus and lymph nodes with extensive infiltration into the sigmoid colon. As she remained free from anaemia, another course of carboplatin was planned to treat her disease without epoetin alfa support. This treatment regimen was abandoned after the first cycle owing to considerable haemotoxicity (neutropenia and thrombocytopenia). It also caused a fall in Hb to 9.4 g/dL but,

when stopped, this recovered to levels higher than those reported before epoetin alfa therapy was administered (>10 g/dL).

Breast cancer

Case 1

Cancer of the right breast (classified as T2, N1, M0, Grade 2 severity, oestrogen receptor (ER) positive) was confirmed for Mrs R. when she was 50 years of age. She was a school secretary who lived with her retired husband. She had three children and there was no history of cancer in her family. She was hypertensive although this was adequately controlled with atenolol.

Initial treatment with a combination of radiotherapy and tamoxifen was successful but 6 months later the cancer returned (classified as T3, Grade 2, ER positive). Mastectomy of the right breast was considered mandatory followed by cyclophosphamide–methotrexate–fluorouracil therapy. By the third cycle it was necessary to reduce the dose of chemotherapy by 20% as she was neutropenic and had an infection. Her Hb also fell from values of 11.9 and 12.8 g/dL recorded pretreatment, to 11.0 g/dL at the start of the third cycle and 10.5 g/dL during the third, when blood transfusion was considered but not administered.

Administration of 10 000 units of epoetin alfa three times a week under the conditions of a clinical trial commenced during the third cycle and continued for 4 weeks after the end of chemotherapy. Before treatment with epoetin alfa Mrs R. felt extremely tired, but after 4 weeks her consultant observed a significant increase in her energy level which coincided with an increase in her Hb to 13.2 g/dL. Subjectively, Mrs R. felt much improved, believed that she had returned to her 'old self' and was looking forward to joining her husband in retirement. Her energy levels measured using a QoL linear analogue scale increased by 10% after 4 weeks treatment with epoetin alfa, and her ability to perform daily activities and her QoL improved by 20%.

Case 2

Mrs J. is a 49-year-old married lady with a family history of cancer. Investigations following mastectomy of the right breast and axillary clearance showed no further disease. She received postoperative adjuvant treatment with tamoxifen for 8 years and remained well for three further years before she noticed a bony swelling over her left temple. An isotope scan subsequently identified additional bony metastases in the pelvis and both femora, and treatment with tamoxifen was reintroduced.

Five months later she reported increasing pain in her left shoulder and clinical examination and a computerized tomography (CT) scan confirmed lymphadenopathy in the left supraclavicular fossa. This resolved following radiotherapy and administration of anastrozole. However, during tumour restaging (8 months after the lymphadenopathy had first been confirmed), CT scans identified a mass in the medial left breast associated with internal mammary chain nodes, axillary nodes, para-aortic and mediastinal lymphadenopathy, and liver metastases.

This lady was depressed despite the support of her husband and her own efforts to overcome her fear of cancer. She was in pain, tired and lethargic, and lacked motivation.

Mrs J. then underwent six cycles of fluorouracil–epirubicin–cyclophosphamide and, within the conditions of a clinical trial, her husband administered 10 000 units of epoetin alfa three times a week. She tolerated chemotherapy very well and there were no palpable masses at the end of the final cycle. Mrs J.'s Hb at the commencement of epoetin alfa was 9.9 g/dL. Administration of epoetin alfa continued for 4 months during which her Hb increased to 10.3 g/dL after 3 weeks, 11.2 g/dL after 7 weeks, 12.2 g/dL after 9 weeks, 12.6 g/dL after 13 weeks and 12.7 g/dL after 18 weeks.

At the end of 4 months treatment with epoetin alfa, Mrs J. felt and looked better, had more energy and was physically more capable. The QoL linear analogue scales used in the trial and completed before epoetin alfa was given scored very low on levels of energy (15%), ability to perform normal daily activities (15%) and overall QoL (25%). However, after 4 weeks administration, these had all increased by 50% and this improvement was maintained throughout the remainder of the trial.

CASE REPORTS OF HAEMATOLOGICAL TUMOURS

Myeloma

Case 1

Mrs W., a 59-year-old retired cook, was diagnosed as having breast cancer, for which she received surgery and radiotherapy and made a good recovery. Six years later, she developed IgA myeloma, which was treated with vincristine–adriamycin–dexamethasone. Mrs W. responded well to this treatment, the cancer went into remission and she was maintained on interferon for 1 year thereafter.

She relapsed 3 years after the diagnosis of myeloma and was pale and weary on presentation. One feature of her relapse was profound anaemia, and her feelings coincided with a fall in Hb from 11.9 to 4.4 g/dL. Treatment with high-dose dexamethasone followed by cyclophosphamide and prednisolone partially suppressed the disease, but she required blood transfusions and received 29 units of blood over the following 6 months. At this time, her Hb fluctuated between 5.6 and 11.1 g/dL, her quality of life was poor, her life was centred on the blood transfusions and she was exhausted by the repeated visits to hospital.

Treatment with epoetin alfa was therefore considered and commenced at 10 000 units three times per week. Her transfusion requirement during the following 6-month period was reduced to 19 units of blood and 2 years later was reduced by over one-third to 9 units over 6 months. The dose of epoetin alfa was not reduced, but with fewer blood transfusions and a greater feeling of well-being Mrs W. has a comfortable QoL and is again able to go on overseas holidays.

Case 2

Mr S. is a 76-year-old retired nuclear worker who enjoys a round of golf. He presented with light-chain myeloma for which he was prescribed melphalan and prednisolone. He also had a history of chronic renal failure and angina, and 12 months after presentation he suffered a myocardial infarction from which he made a good recovery. Four years later his angina had worsened. It was exacerbated by the slightest exertion and he was unable to manage a single flight of stairs without becoming exhausted. Everything he did was an effort and, with regret, he allowed his golf club membership to lapse.

At review, blood tests showed that his Hb was 7.1 g/dL. He was treated with cyclophosphamide and prednisolone and given four transfusions, each of 3 units of blood, at intervals of 3–4 weeks. During this period he remained anaemic with a Hb around 9 g/dL. The blood transfusions temporarily improved his condition and relieved his lethargy, but 2 weeks after each procedure he reported feeling fatigued and anergic.

Mr S.'s Hb was still low at 8.6 g/dL about 6 months later and he was therefore prescribed epoetin alfa 10 000 units three times per week. His anaemia responded well; after 2 weeks his Hb had risen by 2.2 g/dL and within 8 weeks his Hb was above 15 g/dL.

After 6 months of treatment with epoetin alfa, Mr S. no longer suffered from angina and claimed to 'feel wonderful'. His body language mirrored how well he felt and, from being pallid and sluggish, he was pink with vivacity. He reported that he had been on a 3-mile walk and had renewed his membership at the golf club. His dose of epoetin alfa has since been reduced to 4000 units three times per week and his Hb maintained between 14 and 15 g/dL.

Lymphoma

Case 1

Mr B. was 79-years of age when he presented with a 10-day history of malaise, night sweats and generalized weakness. The lymphadenopathy, diagnosed 3 months previously, had spread and was apparent bilaterally in the supraclavicular fossa, axillae, groin and femoral region. In addition, he had hepatosplenamegaly, swollen ankles and cold sores around his mouth. Blood tests revealed an elevated erythrocyte sedimentation rate, thrombocytopenia, a white blood cell (WBC) count of 13.3×10^9/L, and a Hb of 11.8 g/dL. Histological examinations of biopsy tissue identified high-grade aggressive Non-Hodgkin's lymphoma (NHL) of T-cell origin.

Without treatment, Mr B.'s prognosis was very poor and so prednisolone–mitroganterone–etoposide–cytosine–bleomycin–cyclophophamide every 2 weeks was introduced with extreme caution because of his age. Examination 3 weeks later showed a good response to the first cycle. The second cycle was delayed owing to low WBC and granulocyte counts, and the only palpable disease at the start of this cycle was a slightly enlarged liver. He was in complete remission at the end of the third cycle and blood counts were within the normal range after the final cycle.

A month later Mr B. returned to the clinic with a swelling in his neck; the lymphadenopathy had returned in the parotid and cervical regions and axillae. His Hb was 11.0 g/dL and he did not respond to oral chlorambucil. At the request of his relatives for treatment, chemotherapy was begun with methotrexate and carboplatin. His Hb began to fall and, when it had reached 7 g/dL, he was transfused with 4 units of blood. Mr B. felt miserable. He was out of breath and, consequently, his mobility was restricted, so much so that he required a wheel chair to get about.

Treatment with epoetin alfa 10 000 units three times weekly was added to his regimen. His Hb increased to 11.7 g/dL during the next 3 months and fluctuated between 11.9 and 12.8 g/dL during the next 8 months. Sadly he died 10 months later.

This patient tolerated chemotherapy very well and despite a poor prognosis he was in complete remission after the third treatment cycle. He relapsed and needed

blood transfusion and epoetin alfa. Following the introduction of epoetin alfa, Mr B. felt 'on top of the world' and his family was more able to cope and accept his situation because he was both looking and feeling better. In addition, he no longer needed a wheelchair and was able to carry out activities associated with normal living for the last months of his life.

Case 2

Mr L. is 66-years of age and recently retired. He first presented with lethargy, tiredness, breathlessness and headache, and was anaemic with a Hb of 8.2 g/dL. A biopsy showed 99% lymphoma involvement with the bone marrow and he was diagnosed with lymphoplasmacytoid NHL.

Initial treatment included idarubicin and chlorambucil, administered monthly for 6 months, and 2–3 units of blood transfused every 3 weeks. Six months later, lymphoma involvement in the bone marrow had reduced to 65% but his Hb had also fallen to 7.3 g/dL. The first of five monthly cycles of an alternative cytotoxic regime (cyclophosphamide–vincristine–adriamycin–methylprednisolone) was initiated. Mr L. agreed to participate in a clinical trial and was randomized to receive epoetin alfa 10 000 units three times a week for 4 weeks, followed by 23 000 units three times a week for 5 months. His Hb increased and remained within the range of 10.5–14.6 g/dL (mean 12.2 g/dL) over the next 6 months. Although levels were sustained between 13.5 and 14.6 g/dL for 3 months after epoetin alfa had been discontinued, they subsequently fell to between 7.1 and 10.5 g/dL over a period of 4 months when blood transfusions were again considered to be necessary.

Mr L. consented to participate in a trial on the basis that, eventually, commercial availability of epoetin alfa might provide an alternative to blood transfusions: a procedure which disrupted his life because it necessitated frequent visits to hospital and took up much of his spare time. Although he felt faint after the first injection, he considered that participation had been very worthwhile. This was confirmed by his answers to the QoL questionnaire used in the trial which reported 43% 'improved' responses, 49% 'unchanged' responses and 8% 'worse' responses to a total of 94 questions.

Leukaemia

Case 1

Mr D. was 66-years old when he was referred with Hb, WBC and platelet counts of 9.2 g/L, 1.9×10^9/L and 13.0×10^9/L respectively. His medical history included a hernia repair, appendectomy and pleurisy. A diagnosis of acute myeloid leukaemia (AML) was made from the results of the referral bone marrow biopsy, which was hypercellular with undifferentiated blast cells, and a subsequent biopsy that showed evidence of myelodysplasia.

He responded well to treatment involving three cycles of daunorubicin and cytarabine and was in remission after the first course. A further bone marrow biopsy after the third cycle showed that marrow regeneration was extremely slow. He remained pancytopenic; his Hb, WBC and platelet counts were 10.8 g/dL, 1.6×10^9/L and 25.0×10^9/L, respectively, and so chemotherapy was discontinued. Blood transfusions were considered necessary and, because of his age and because he lived some distance from the hospital, these were given when his Hb had fallen to 9 g/dL. Initially he required 2 units of blood every 2–3 weeks, but this was subsequently reduced to 2 units a month.

Mr D. did not feel particularly well; his mood was low, he disliked relying on others and was unable to do what he wanted. As his Hb remained low (between 9.2 and 9.5 g/dL), the decision was made to stop the blood transfusions and to start treatment with epoetin alfa at 10 000 units thrice weekly. Venesection to reduce ferritin levels caused by multiple blood transfusions and epoetin alfa therapy continued over the next 12 months during which Hb values of between 10.1 and 12.5 g/dL were recorded.

Mr D. was by nature a very independent character and managed his own business. At diagnosis, he complained of lassitude and limited exercise tolerance and slept frequently during the day, a profile which, owing to his independent nature, led to clinical depression. The need for frequent visits to hospital for blood transfusions prevented him using his holiday home, causing further despondency. At the start of treatment with epoetin alfa, he remained very dubious that his life-style would return to normal. In practice, however, the administration of epoetin alfa significantly improved his life; he returned to his 'old self' – buoyant, self-motivated and independent – and to his work. Furthermore, as he was competent to self-inject epoetin alfa, he was able to resume vacations at his holiday home.

Case 2

Mr W. was diagnosed as suffering from AML at the age of 61 years and treatment with daunorubicin and cytarabine was initiated immediately. The disease was still virulent

after the first two cycles and treatment was changed to high-dose cytarabine. His WBC count fell to 0.2×10^9/L and, as there was little subsequent evidence of bone marrow recovery, chemotherapy was discontinued.

At this time and over a period of 4 weeks, Mr W.'s Hb had fluctuated between 9.2 and 10.8 g/dL. Blood transfusions were considered necessary during the next 5 months; 3 units of blood on each of nine occasions for the first 3 months (Hb between 8.7 and 11.1 g/dL) and 2 units on each of four occasions for months four and five (Hb between 10.1 and 11.7 g/dL). Towards the end of this period, a bone marrow biopsy revealed evidence of decreased erythropoiesis and number of megakarocytes, and the presence of 3% blast cells.

The original cytogenic abnormality was still present in 20% of the cells and, despite the potential for relapse, a decision was made not to risk further chemotherapy. Hb at this time was around 10.5 g/dL.

Treatment with epoetin alfa 10 000 units three times a week was considered to be of possible benefit. Four weeks after the start of treatment with epoetin alfa, Hb had risen by 2 mg to over 13 g/dL and venesection was considered necessary. During the remainder of the 12-month treatment period, Hb fluctuated between 12.4 and 15.1 g/dL, around a mean value of 14.1 g/dL.

Mr W. experienced transient flu-like symptoms when he initially began injections of epoetin alfa. This he managed by administrating the treatment before lying down at night. In addition, he had had a fear of needles and was apprehensive of administering epoetin alfa himself. Once shown the procedure, however, he admitted surprise at the ease of self-administration and lost this fear as his QoL improved.

Mr W., a company director, was very concerned about the amount of time he spent away from his business when in hospital for blood transfusions. He felt that epoetin alfa had given him his freedom and now lives a normal life. He uses his motor home that had become too heavy to drive and is able to travel away from the constraints of the hospital.

DISCUSSION

The aim of these case studies is to add the benefit of our personal experience to the body of clinical trial literature, to demonstrate the ways in which anaemic patients with cancer may benefit from epoetin alfa. Such case studies can never substitute for good clinical trial data but should be considered alongside more detailed accounts of epoetin alfa, particularly those after release into community practice. However, they offer the practical details and personal aspects, which are so often lacking in reports of clinical studies.

These case reports effectively describe the effects that anaemia can have on patients with cancer, the disruption to normal daily life from fatigue and frequent hospital visits for blood transfusions, and the resulting problems for the patient's family.

Despite differences in the primary tumour site, patients generally complained of fatigue, lethargy and of being tired or 'washed out'. They lacked motivation and energy to carry out every-day domestic tasks and social activities such as walking, gardening and playing golf. Restrictions in lifestyle led to frustration, irritability and depressed mood. The patient's family was also affected. Their role as carers was extended to include tasks once accomplished by the patient and providing transport to hospital. They found it more difficult to accept that a relative had cancer and to cope with the side-effects of chemotherapy. Both patients and carers complained about the length of time spent travelling and attending hospital appointments for blood transfusions that added to the patient's exhaustion.

In all cases, epoetin alfa increased Hb to clinically acceptable levels, concurring with the results of clinical trials that studied the effects of the administration of epoetin alfa to anaemic patients with cancer receiving cyclic chemotherapy regimens that did and did not contain cisplatin (Platanias *et al*. 1991; Miller *et al*. 1992; Abels 1993; Cascinu *et al*. 1993, 1994; Case *et al*. 1993; Henry *et al*. 1994, 1995; Littlewood *et al*. 1999). In two controlled open-label trials each involving over 2000 patients in community-based practices, patients were treated with 10 000 units (150 Units/kg) subcutaneously thrice weekly that could be adjusted according to Hb response (Glaspy *et al*. 1997; Demetri *et al*. 1998). Patients responded to epoetin alfa equally well across all tumour types, with a response time of between 51 and 54 days (Demetri *et al*. 1998), attaining maximum Hb at 3–4 months (Glaspy *et al*. 1997; Demetri *et al*. 1998), and with a mean increase of around 2 g/dL from baseline to final Hb (Glaspy *et al*. 1997; Demetri *et al*. 1998).

Many studies have shown a correlation between a positive response to epoetin alfa treatment and improved QoL (Abels 1993; Case *et al*. 1993; Pedrazzoli *et al*. 1993; Leigeb *et al*. 1994; Rose *et al*. 1994; Henry *et al*. 1995; Ludwig *et al*. 1995; Glaspy *et al*. 1997; Demetri *et al*. 1998; Cleeland *et al*. 1999; Littlewood *et al*. 1999). However, disease response from chemotherapy is also associated with improved QoL (Coates *et al*. 1987; Cella & Bonomi 1995) and this could confound the absolute impact of epoetin alfa on QoL improvement. Neverthe-

less, favourable improvement in QoL caused by epoetin alfa treatment using linear analogue scales (Glaspy *et al*. 1997; Demetri *et al*. 1998) and the Functional Assessment of Cancer Therapy-Anaemia questionnaire (Demetri *et al*. 1998) has been reported, regardless of disease response to chemotherapy. A direct and significant correlation was demonstrated between changes in Hb and QoL (Glaspy *et al*. 1997; Demetri *et al*. 1998) that mirrored the expected relationship between disease response and QoL (Demetri *et al*. 1998). The greatest incremental QoL improvement was observed when Hb was increased by epoetin alfa from 11 to 12 g/dL (range 11–13 g/dL) (Cleeland *et al*. 1999).

These case reports support observations that suggest beneficial effects of epoetin alfa therapy on functional status and QoL in anaemic patients with cancer treated in clinical trials and community-based practices. Treatment was seen to cause relatively large changes in QoL in this case series (assessed verbally and using linear analogue scales), a magnitude of effect in concordance with the significant improvements recorded as medium to large effects on energy levels, activity levels and overall QoL by Glaspy *et al*. (1997). Previously predicted effects (Curt *et al*. 1999) on caregivers were revoked.

Similar increases in QoL were observed in patient's who self-administered epoetin alfa and in those for whom epoetin alfa was administered by a health care professional (Glaspy *et al*. 1997). In two cases, the benefits of self-injection of epoetin alfa were specifically mentioned by patients, notably better attendance at work and the freedom to go on holiday. In addition, the favourable safety profile of epoetin alfa was confirmed in these case histories. Adverse effects experienced by patients were consistent with the underlying disease state and chemotherapy.

Epoetin alfa is a new standard of treatment. Self-administration allows patient's to lead a normal lifestyle, they report a higher QoL than those receiving placebo plus transfusions (Cascinu *et al*. 1993) and increases in Hb tend to be maintained. The initial recommended dose is 10 000 units (equivalent to 150 units/kg body weight in an average person) subcutaneously three times a week for 4 weeks, thereafter modified with respect to Hb. Data support an early evaluation of epoetin alfa effect after 1 month of treatment to determine patient response (Glaspy *et al*. 1997; Demetri *et al*. 1998). An increase in dosage may be necessary to achieve a meaningful increase in Hb and QoL. Later evaluations can be used to determine a maintenance dose.

The negative impact of anaemia on functional status of patients during cancer chemotherapy and the potential for increased QoL in these patients by aggressive treatment of anaemia is underestimated. QoL was enhanced by epoetin alfa even in view of chronic disease and intensive chemotherapy. Such improvement is also meaningful to families of patients with cancer who often provide support during treatment.

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