Epoetin in cancer-related anaemia

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Abstract Cancer-related anaemia has a number of causes, not least the underlying malignancy itself which plays a role in suppressing erythropoiesis. Anaemia is often exacerbated by cancer treatments, in particular routinely used cytotoxic chemotherapy. Chronic anaemia of cancer is often characterized by inappropriately low levels of endogenous erythropoietin for the degree of anaemia, and manifests clinically with generalized hypoxia and resultant severe fatigue. Epoetin alfa is one recombinant form of erythropoietin, the primary human growth factor responsible for promoting proliferation and survival of erythroid progenitor cells. Epoetin alfa has been widely studied for the treatment of anaemia associated with renal failure and is now recognized as having significant potential in the management of cancer-related anaemia. Studies suggest that epoetin alfa is an effective treatment in a proportion of cancer patients with symptomatic anaemia. It also appears useful for the prevention of chemotherapy-induced anaemia. Studies in a number of different cancer settings have shown that epoetin alfa significantly increases haemoglobin and haematocrit, reduces transfusion requirements and improves quality of life for the patient.

Key words: anaemia; cancer; epoetin; fatigue; haemoglobin; quality of life

Introduction

In cancer, anaemia is a common haematological abnormality arising as a result of contributing factors such as the underlying chronic disease, chemotherapy, radiation therapy or bone marrow invasion with tumour. Fatigue due to hypoxia is undoubtedly the primary symptom of cancer-related anaemia, causing a significant reduction in physical functioning, mental health and overall quality of life for the patient. Anaemia may even adversely affect the patient’s response to cancer treatment.

Anaemic cancer patients have a pathophysiology similar to anaemic patients with end-stage renal disease, in that endogenous erythropoietin is inappropriately low for the degree of anaemia. Such observations suggest that therapy with epoetin alfa might offer a means of reversing anaemia in cancer patients. In recent years, there has been a burgeoning interest in the use of epoetin alfa to treat, and possibly to prevent, anaemia associated with both solid tumours and haematological malignancies. This review article summarizes the background and presents recent findings and progress in this field.

Cancer-related anaemia

Pathophysiology

Anaemia associated with cancer has several possible causes and contributing mechanisms, which may be present concomitantly (Table 1) [1]. In addition to factors which cause red blood cell loss and diminished red blood cell production, other factors involved include interventions such as radiation therapy and chemotherapy with cytotoxic drugs. For example, many cytostatic agents are known to cause a reduction in endogenous erythropoietin production, thus inducing anaemia as a side effect of treatment [2,3].

Anaemia, however, occurs most commonly as a result of the malignancy itself, and is referred to as ‘chronic anaemia of cancer’ [1]. Intense interaction between the tumour cell population and the host’s

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immune system appears to lead to an increase in the levels of cytokines such as interferon-\(\gamma\), interleukin-1 and tumour necrosis factor [1,3]. This upsurge of inflammatory cytokines brings about a chronic anaemia by suppressing the differentiation of erythroid precursors in the bone marrow, reducing erythropoietin production and preventing normal utilization of iron [1]. Additionally, tumour cells produce an ‘anaemia-inducing substance’, thought to be responsible for the decreased life-span of red blood cells noted in some patients with cancer-related anaemia [1]. Chronic anaemia of cancer is also exacerbated by chemotherapy [4].

**Incidence and clinical presentation**

The incidence of chronic anaemia in cancer patients depends on malignancy type, stage and duration, treatment regimen and the presence of any intercurrent infection. In colorectal and breast cancer, for example, the prevalence of severe anaemia (haemoglobin \(\sim 8\) g/dl) is relatively low (10–20%); contrast this with patients who have non-Hodgkin’s lymphoma or multiple myeloma, or those receiving chemotherapy for ovarian or lung cancer, where the prevalence appears to be far higher (50–60%) [5].

Anaemia in cancer patients usually manifests clinically as hypoxia-related impairment of virtually every organ system [1]. Symptom severity is dependent on the degree of anaemia, its speed of onset, the underlying malignancy and the patient’s cardiovascular and pulmonary function. For the patient, severe fatigue, physical debilitation and resultant feelings of depression are probably the key symptoms.

There is no doubt that symptomatic anaemia and the fatigue it brings can be devastating for a cancer patient, whose quality of life will be reduced further on the physical, social and emotional levels [4].

**Management of cancer-related anaemia**

**Rationale for treatment**

All cancer patients with symptomatic anaemia of cancer should be treated in an attempt to offset the detrimental effects of the anaemia on their physical activities, emotional well-being and on the final outcome, particularly in terms of their response to anticancer treatments. Despite the obvious rationale, the negative impact of anaemia on quality of life for a cancer patient often remains underestimated, and many cancer patients with anaemia who could benefit from some form of treatment are managed inadequately, or not at all [1].

**Overview of treatment options**

Treatment decisions should always be based on symptoms and laboratory findings. Options include the use of blood transfusions, iron supplementation and therapy with epoetin alfa.

Blood transfusion can have an immediate beneficial effect and is of value if the anaemia is life-threatening or patients fail to respond adequately to treatment with epoetin. However, blood transfusions carry several recognized risks which must be taken into account when deciding on treatment [1].

Epoetin alfa has been used successfully in recent years to correct or improve symptoms in anaemic cancer patients. It can stimulate erythroid activity and is particularly beneficial in those patients with a blunted erythropoietin response to hypoxia [1]. Clinical studies have proved that epoetin alfa can ameliorate the anaemia associated with cancer and chemotherapy, reduce the need for blood transfusions and improve quality of life [6]. For a patient who responds, epoetin offers an effective treatment for anaemia; however, not all cancer patients respond well to therapy.

Patients who are deficient in iron require iron supplementation, but neither oral nor parenteral iron is particularly effective as monotherapy for the anaemia of cancer. Iron supplementation combined with epoetin is more effective than iron alone; parenteral iron administration has been shown to improve the response to combined treatment to a greater extent than oral iron administration [7].

**Focus on epoetin**

**Clinical benefits in cancer-related anaemia**

Epoetin alfa can be used to treat patients with symptomatic cancer-related anaemia with the intention of relieving symptoms and improving physical performance and feelings of well-being. Epoetin alfa has also been administered prophylactically in an attempt to prevent or postpone chemotherapy- or radiotherapy-induced anaemia. Prevention of anaemia during anticancer treatment may enable use of higher doses of chemotherapy and may improve outcome for patients undergoing radiotherapy [2].

The available clinical evidence clearly supports the use of epoetin alfa to combat cancer-related and chemotherapy-induced anaemia by increasing the haematocrit and haemoglobin, decreasing transfusion requirements and improving quality of life generally [6].

Improvement in exercise duration and oxygen consumption was demonstrated during epoetin alfa therapy in patients with anaemia due to renal failure [8], and similar findings have been reported in cancer patients. For example, in multiple myeloma patients who responded to 12 weeks’ epoetin alfa treatment, an improvement in performance was noted, based on WHO performance criteria [9]. This improvement was not seen in patients who were classified as epoetin alfa ‘non-responders’.

Quality-of-life assessments have also shown a significant improvement in mood, appetite and general well-being in one group of cancer patients responding to 12 weeks’ epoetin alfa treatment. Significant correlations were noted between haemoglobin and degree of
improvement in mood and appetite (Figure 1) [10]. These findings suggest that achieving haemoglobin within the normal range has a beneficial effect on life quality for patients with cancer-related anaemia [2].

**Use in chemotherapy-induced anaemia**

Patients with cancer have been shown to have inappropriately low endogenous erythropoietin for the degree of anaemia. Further suppression of erythropoiesis results from chemotherapy [4]. Epoetin has been studied in the treatment and prevention of chemotherapy-induced anaemia in cancer patients.

**Treatment studies.**

A number of randomized, placebo-controlled studies [4] have investigated the effect of epoetin in treating anaemic cancer patients (with haemoglobin <10.5 g/dl) categorized as follows:

- receiving no chemotherapy; given epoetin alfa 100 IU/kg or placebo subcutaneously (s.c.) three times weekly for 8 weeks.
- receiving non-cisplatin-based chemotherapy; given epoetin alfa 150 IU/kg or placebo s.c. three times weekly for 12 weeks.
- receiving cisplatin-based chemotherapy; given epoetin alfa 150 IU/kg or placebo s.c. three times weekly for 12 weeks.

In these studies, 'response' was defined as improving the haematocrit by 6% or more, unrelated to transfusion. In each group (no chemotherapy, non-cisplatin chemotherapy, cisplatin chemotherapy), epoetin alfa-treated patients responded to a significantly greater extent than placebo-treated patients ($P<0.008$). The improvement in anaemia in all three groups was reflected in reduced transfusion requirements in epoetin alfa-treated patients and in the units transfused per patient. Importantly, transfusions in both groups receiving chemotherapy were significantly reduced by epoetin alfa ($P<0.005$) when compared with the placebo-treated patients. There was also a lag phase before the beneficial effect became apparent (Figure 2) [4].

After the initial double-blind treatment phase, open-label epoetin alfa could be prescribed with dose increments of 50 IU/kg, to a maximum of 300 IU/kg, depending on haemoglobin response. When total epoetin alfa exposure was examined, 40% of the no chemotherapy group, 56% of the non-cisplatin chemotherapy group and 58% of the cisplatin chemotherapy group were found to have responded with haematocrit increases of >6% unrelated to transfusions. Over 6 months of treatment, the corresponding numbers of patients transfused decreased from 31.4 to 10.3% in the no chemotherapy group; from 25.2 to 13% in the non-cisplatin chemotherapy group and from 42.7 to 11.5% in the cisplatin chemotherapy group (see Figure 2) [4].

Recently, a large community-based study conducted by Glaspy et al. [11] investigated the therapeutic benefits of epoetin alfa in >2000 patients with anaemia related to both solid and haematological tumours. Treatment was administered for a 4 month period at a dose of 150 IU/kg, given s.c., three times a week; the dose could be increased to 300 IU/kg if haematocrit response proved inadequate [4,11]. Of the total patient population, 22% were receiving cisplatin-based regimens, 18% carboplatin-containing regimens and the remaining 60% were receiving non-cisplatin-based cyclical chemotherapy [4].

Haemoglobin improved significantly ($P<0.001$) in all tumour response categories, even in patients with progressive disease. Epoetin alfa was associated with a 50% decrease in both the proportion of patients requiring transfusion and the number of units transfused per patient per month (Figure 3) [4]. Epoetin alfa was also associated with significant increases in mean self-rated scores for energy, activity and overall quality of life; these improvements correlated with the increase in haemoglobin and were independent of tumour response [11]. Epoetin alfa was well tolerated in this study.

The findings from these clinical studies indicate that epoetin alfa is effective in improving functional status and quality of life in anaemic cancer patients receiving...
due to chemotherapy and reduce the prospective need for blood transfusions. A randomized study in patients with small cell lung cancer (receiving up to six cycles of chemotherapy) investigated the benefits of epoetin alfa in preventing anaemia when given at s.c. doses of either 300 or 150 IU/kg, three times a week [4]. Treatment was compared with an untreated control group. Epoetin alfa was given throughout chemotherapy, starting the day after chemotherapy and continuing until 3 days before the next cycle. Epoetin alfa lessened the decline in haemoglobin and reduced the requirement for transfusions in small cell lung cancer patients who initially were non-anaemic and were undergoing primarily cytotoxic chemotherapy [4].

In another study, 62 early-stage breast cancer patients undergoing six cycles of accelerated adjuvant chemotherapy were randomized to receive either epoetin 150 IU/kg three times a week or no additional treatment. Throughout the chemotherapy, epoetin-treated patients maintained stable haemoglobin, whereas control patients developed a progressive anaemia. At the end of chemotherapy, epoetin-treated patients showed a mean decrease in haemoglobin of 0.8 g/dl, compared with 3.05 g/dl in the control group. Clinically significant anaemia (haemoglobin ≤10 g/dl) was seen in 52% of the control group but in none of the epoetin-treated patients [12].

Thus, studies have confirmed that epoetin alfa 150 IU/kg, given s.c. three times a week, can effectively treat chemotherapy-induced anaemia in cancer patients and can also help prevent anaemia developing in initially non-anaemic patients receiving cancer chemotherapy. Of key importance is the fact that the epoetin-induced improvements in haemoglobin and haematocrit markedly reduce the need for red blood cell transfusions.

Use with high-dose chemotherapy

High-dose chemotherapy followed by bone marrow transplantation (BMT) or peripheral blood stem cell (PBSC) support is used increasingly in the treatment of haematological malignancies and some solid tumours [13]. High-dose chemotherapy aims to treat the cancer with a high concentration of chemotherapeutic agents in an attempt to overcome drug resistance problems. Unfortunately, high-dose chemotherapy induces profound myelosuppression as a toxic side effect and, even when prognosis is improved by bone marrow or PBSC support, there is still likely to be leucopenia, thrombocytopenia and severe anaemia such that packed red blood cell and platelet transfusions frequently are required.

Following high-dose chemotherapy, anaemia will develop and serum erythropoietin will increase, although the course of the anaemia and the changes in serum erythropoietin are different dependent on whether patients receive allogeneic (genetically different) BMT or autologous (patient-donated) BMT [13]. Epoetin in the treatment and prevention of anaemia has been studied in these settings.
Treatment with epoetin in the allogeneic BMT recipient after high-dose chemotherapy has been found to be effective, whereas treatment in the autologous BMT recipient has proved disappointing. When outcomes from both allogeneic \((n=10)\) and autologous \((n=10)\) BMT patients receiving epoetin \(75 \text{IU/kg/day for 30 days}\) after high-dose chemotherapy were compared with matched historical controls, the red blood cell transfusion requirement in the allogeneic BMT recipients was less than half that of controls \((P<0.001)\), whereas transfusion requirements in autologous BMT recipients was similar to controls \((P=0.44)\) [14].

The efficacy of epoetin in allogeneic BMT recipients has been confirmed in other studies. In one example, 50 patients with haematological malignancies treated with high-dose chemotherapy and allogeneic BMT received either placebo or epoetin, 200 IU/kg/day intravenously \((i.v.)\) for 4 weeks, then 200 IU/kg twice weekly \(i.v.\) for the next 4 weeks. Haemoglobin was similar in both groups during the study period, but the epoetin-treated patients required fewer blood transfusions to maintain the same haemoglobin compared with patients given placebo \((5 \text{ RBC U/person vs 10 RBC U/person respectively, } P=0.04)\) [15].

Since bone marrow often is unable to respond to epoetin after high-dose chemotherapy in autologous BMT recipients, it may be more effective to administer epoetin while the marrow is still responsive, i.e. before the chemotherapy. In one small study, patients received either placebo \((n=9)\) or epoetin \((n=7)\), 10 000 IU/day \(s.c.\) for 7 days immediately before high-dose chemotherapy, then the same dose for 7 days after chemotherapy. Haemoglobin after chemotherapy was comparable in both groups but the transfusion requirement for the epoetin group was 0.57 RBC U/patient compared with 4.0 RBC U/patient in the placebo group \((P<0.05)\) [16].

Thus, several studies support the use of epoetin to correct the anaemia associated with allogeneic bone marrow transplantation following high-dose chemotherapy. In patients receiving autologous bone marrow, epoetin appears ineffective in the early stages. In delayed anaemia \((\text{later than 30 days after high-dose chemotherapy})\), epoetin may be useful in both allogeneic and autologous BMT recipients [13]. When given before high-dose chemotherapy, epoetin can reduce transfusion requirements before significant myelosuppression occurs and there is also some evidence to suggest that epoetin may help mobilize erythroid progenitor cells and other precursor cells in this setting [13]. Thus, epoetin has an important role to play in the treatment of anaemia associated with high-dose chemotherapy.

**Use in anaemia associated with haematological cancers**

**Myeloma and lymphoid malignancies.**

One initial study in a group of 13 anaemic myeloma patients used epoetin alfa at a dose of 150 IU/kg three times a week, which was increased incrementally to a maximum of 250 IU/kg if no response was observed [9]. A response to epoetin alfa treatment was seen in 11 \((85\%)\) patients, who had an increase in haemoglobin concentration of at least 2 g/dl. The median time to response was 5 weeks. These responders displayed a significant increase in reticulocyte counts without any effect on leucocyte or platelet counts. The bone marrow erythropoietic compartment increased by \(~50\%)\.

Epoetin treatment was well tolerated and improved quality of life for those who responded.

A number of other studies have confirmed that epoetin is effective in increasing haemoglobin and correcting anaemia in a significant proportion of patients with lymphoid malignancies [17,18]. This effect appears independent of concomitant chemotherapy. In all the trials to date, epoetin has proved well tolerated, with no clinically relevant side effects [19]. In particular, these cancer patients did not report the episodes of hypertension sometimes associated with epoetin use in patients with anaemia of chronic renal failure. In myeloma patients, monoclonal and other components have not been affected by epoetin therapy, and no effects on myeloma growth have been noted in any clinical study [19].

**Chronic lymphocytic leukaemia.**

Anaemia in patients with chronic lymphocytic leukaemia \((\text{CLL})\) is not thought to be the result of inadequate erythropoietin production, but is rather due to haemolysis or splenic sequestration of red blood cells [19]. Despite this, some studies have investigated epoetin for the treatment of anaemia in \(\text{CLL}\) and have demonstrated benefit in a proportion of these patients [19]. For example, Rose et al. [20] randomized 221 anaemic \(\text{CLL}\) patients into two groups: a placebo group and a group receiving epoetin alfa 150 IU/kg \(s.c.\), three times a week for 12 weeks. The chemotherapy regimen was identical between the two groups. After 12 weeks’ therapy, an increase in haematocrit of at least 6% unrelated to transfusion was noted in 47% of the epoetin alfa-treated group compared with only 15% of the placebo group \((P<0.001)\). Thirty two percent of the epoetin alfa-treated patients reached a haematocrit of at least 38% compared with only 5% in the placebo group \((P<0.001)\). Units transfused were significantly reduced in epoetin-treated patients vs placebo. Quality of life (measured by energy, self-rated health, physical and social function and mental health) was significantly improved in patients who reached a haematocrit of 38%.

Despite the positive findings from this study, the long-term response, optimal dose regimen and predictors of response remain to be determined for this particular patient group.

**Myelodysplastic syndromes.**

Myelodysplastic syndromes \((\text{MDS})\) are a specific type of haematological malignancy, occurring mainly in the
elderly. Approximately two-thirds of MDS patients present with anaemia, and nearly all experience anaemia during the course of their disease, often becoming transfusion-dependent. The pathogenesis of the anaemia in MDS is complex; erythroid progenitors are defective for their proliferation and maturation, and patients often have high endogenous serum erythropoietin, which is not usual in other cancer-related anaemias. Theoretically, there is a rationale for treating MDS patients with epoetin in an attempt to overcome the defective proliferation with pharmacological doses of epoetin. However, studies have shown rather low responses to epoetin alone (15–40% response) [21]. Combinations with cytokines, such as recombinant human granulocyte colony-stimulating factor, have been tested [22,23], but further studies are required to determine fully whether such combinations might increase response rates in selected MDS patients.

Use with radiotherapy

Anaemic cancer patients have been found to demonstrate a poorer response to cancer treatment, particularly radiotherapy, when compared with non-anaemic patients. Haemoglobin during radiotherapy is positively correlated with patient survival and local control of certain tumour types [24,25]. Haemoglobin has been shown to be a predictor of disease-free and/or overall survival after radiotherapy for cervical and head/neck cancers, independently of other variables [25]. Work has also suggested that a low haemoglobin specifically decreases the efficacy of radiation therapy [24]. It has been postulated that this lack of effect, or ‘radioresistance’, of the tumour cells results from tissue hypoxia [25]. In other words, maintenance of normal tissue oxygenation is necessary to prevent an impaired response to radiotherapy and improve treatment outcome.

One early study demonstrated that red blood cell transfusion prior to pelvic radiotherapy significantly increased the disease-free survival rates of anaemic patients to the level of that of non-anaemic patients [24,25]. The recognition of a clear association between haemoglobin and tumour control by radiation therapy has resulted, in some centres, in severely anaemic cancer patients being transfused routinely prior to a course of radiotherapy. Treatment with epoetin is another possible option.

One study has assessed the effects of epoetin alfa on haemoglobin in 40 patients with a baseline haemoglobin of <13.5 g/dl, scheduled to undergo a 5–8 week course of daily radiation therapy for a solid tumour without metastases [24]. All patients received oral iron and half the group were also given epoetin 150–300 IU/kg s.c. three times a week, beginning 0–10 days prior to the first dose of radiation. All the patients treated with epoetin alfa demonstrated an increase of >6% in haemoglobin during radiotherapy, compared with only two of the 20 control patients (P<0.001). During therapy, haemoglobin rose to a mean of >14 g/dl in 80% of the epoetin alfa-treated group compared with only 5% of the control group (P<0.001). Epoetin alfa treatment had no significant effect on blood pressure, white blood cell, neutrophil or platelet counts, or liver or renal function. This study showed that epoetin alfa, with ferrous sulfate, appears to be an effective means of increasing red cell mass during radiotherapy [24]. Further work is required to determine whether tumour control by radiotherapy is enhanced by adjuvant treatment with epoetin.

Patient selection for treatment

The selection of cancer patients for treatment with epoetin is regarded as mandatory [2], because ~50–60% of unselected patients respond well to treatment [2,3]. A ‘response’ to epoetin is usually defined in terms of normalization of the haematocrit in anaemic cancer patients, or maintenance of a normal haematocrit where epoetin is given to prevent anaemia during chemotherapy [3]. As well as avoidance of blood transfusion in MDS patients, there is certainly a clear dose–response effect with epoetin [3], but doses utilized in cancer patients typically have been higher (in the range 450–900 IU/kg/week) than those recommended in renal failure patients [3]. Responsiveness, then, appears to vary between patients and disease categories, depending on a range of influencing factors. The prediction of response to treatment is, however, feasible.

Variable response.

The response to epoetin in the treatment of cancer-related anaemia has been linked to baseline haematocrit, transfusion needs [4] and tumour type [2], with high response rates noted in patients with head/neck cancers, lung cancer, other squamous cell carcinomas or lymphoproliferative disorders (Figure 4) [2]. However, the influence of tumour type is likely to be

![Fig. 4 Responsiveness of different malignancies to epoetin treatment. CLL, chronic lymphocytic leukaemia; NHL, non-Hodgkin’s lymphoma. (Reproduced with permission from [2]).](image-url)
significant only when there is major marrow involvement and reduced residual haematopoiesis, or if specific mechanisms for anaemia exist (e.g. haemolysis, splenomegaly, bleeding) [4].

Chemotherapy- and/or radiotherapy-induced anaemia appear to respond well to epoetin [2], although it is thought that lower response rates can be expected in patients receiving more intensive chemotherapy regimens [3]. Complications of chemotherapy, such as inflammation, infections, nutritional deficiencies or bleeding, may have a negative impact on response to epoetin [3].

Functional iron deficiency, diagnosed as a percentage of hypochromic red blood cells >10% and/or transferrin saturation <15%, is a major factor limiting response to epoetin therapy. However, since there is concern that some tumour cells require iron for maximal growth, routine iron supplementation of all cancer patients receiving epoetin is not recommended, unless absolute iron deficiency is present [3]. Iron supplements can be given until the percentage of hypochromic red blood cells returns to normal.

The response to epoetin in cancer patients can be slow to develop; for instance, significant differences in transfusion requirements between epoetin- and placebo-treated patients may become apparent after the first month of treatment [3]. Response can be maintained for a year or more, although transient loss of responsiveness has been noted under certain circumstances, for example intercurrent infection, inflammation, surgery or progression of the underlying cancer [2].

**Predicting response.**

As noted previously, ~50–60% of anaemic cancer patients respond well to epoetin therapy [2,3] and response to treatment can take weeks to become clinically apparent; up to 4–8 weeks’ epoetin therapy may be needed to rule out responsiveness in a given patient [2]. Such treatment may be costly and non-productive in a non-responsive patient, hence the focus has been on developing reliable parameters for the prediction of response to epoetin in individual cancer patients.

There have been two main approaches to predicting response. Firstly, analyses have been conducted to determine whether serum erythropoietin is lower than anticipated, based on the patient’s haemoglobin (the degree of blunted erythropoietin response) [2,3]. Secondly, analyses were done to measure predictability of indicators of erythropoietic marrow responsiveness (such as increases in haemoglobin, reticulocyte count, soluble transferrin receptors or serum ferritin) in the initial stages of epoetin treatment [2,3].

One useful predictive model based on measurement of erythropoietin and haemoglobin has shown that if, after 2 weeks of treatment with epoetin, serum erythropoietin is <100 mU/ml and haemoglobin has increased by >0.5 g/dl, a response to epoetin can be predicted with 95% accuracy. Conversely, if serum erythropoietin exceeds 100 mU/ml and haemoglobin has failed to increase by at least 0.5 g/dl, a lack of response can be predicted with 93% accuracy and epoetin treatment should be discontinued [2].

These, and various other, outcome prediction models for epoetin treatment offer the means to ensure cost-effective use of this agent by providing it to as many anaemic cancer patients as possible, with a high chance of a success. Patients should be monitored for infections, functional iron deficiency and other factors that may act to reduce a high predicted response to epoetin [3].

**Conclusions**

Symptomatic anaemia of cancer can cause severe fatigue and a significantly impaired quality of life for the patient. Often, this negative impact of anaemia is underestimated and cancer patients with anaemia are poorly managed. Typically, patients with cancer have inappropriately low concentrations of endogenous erythropoietin for the degree of anaemia and further suppression of endogenous erythropoietin can be induced by cytokines used for chemotherapy. Thus, epoetin offers a potentially beneficial therapy for cancer-related anaemia.

Clinical studies have shown that epoetin alfa (150 IU/kg three times a week) effectively treats a proportion of patients with symptomatic anaemia of cancer and can prevent or reduce treatment-induced anaemia in patients undergoing cancer chemotherapy. Epoetin increases haemoglobin concentration and the haematocrit, reduces the need for blood transfusions and significantly improves quality of life as a direct result. The efficacy of epoetin in the treatment of the anaemia which develops in the setting of high-dose chemotherapy with allogeneic bone marrow transplantation has been demonstrated. Epoetin has also been used with success to treat anaemia in a range of haematological cancers, including the atypical anaemia associated with CLL and, when therapy is combined with other growth factors, in MDS.

Anaemia of cancer has been associated with impaired tumour response to radiotherapy. Normalization of haemoglobin in anaemic cancer patients has been shown to improve local tumour control and disease-free survival after curative radiation treatment. Treatment with epoetin may help improve the tumour response to radiotherapy in certain settings.

It is important to recognize that even 50–60% of unselected cancer patients respond adequately to epoetin. Thus, careful patient selection according to reliable prediction criteria is vital to ensure optimum clinical use of this therapy.

With all these facts in mind, the therapeutic, or prophylactic, use of epoetin should always be considered as an important component of the overall care for cancer patients.
References