

# Effects of Cancer-Related Anemia on Clinical and Quality-of-Life Outcomes

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Although considerable progress has been made in preventing and alleviating many of the common toxicities associated with cancer and its therapy, cancer-related anemia often is overlooked, left untreated, or considered of lesser importance by healthcare providers. Yet anemia may be present in more than half of all patients with cancer (Groopman & Itri, 1999), and evidence suggests that cancer-related anemia plays an important role in key clinical and quality-of-life (QOL) outcomes.

Erythropoiesis, the production of red blood cells, is controlled by the growth factor erythropoietin (EPO), which is produced mainly by the kidneys in response to hypoxia (Cazzola, Mercuriali, & Brugnara, 1997). EPO then is transported to the bone marrow, where it upregulates the processes of survival, differentiation, and maturation of erythroid cells. Other essential requirements for erythropoiesis include vitamin B<sub>12</sub>, folic acid, and iron (Koeller, 1998).

The underlying mechanisms of anemia in patients with cancer are numerous and may be multifactorial in nature. Potential causes include hemorrhage, displacement of bone marrow by malignant cells, damage to bone marrow from previous therapy, hemolysis, nutritional abnormalities, nephrotoxic interventions, myelosuppressive effects of chemotherapy and radiation therapy, and anemia associated with cancer itself (Spivak, 1994). These conditions may lead to impaired EPO production, decreased sensitivity to EPO, and a reduction in erythrocyte progenitor cell numbers (Mercadante, Gebbia, Marrazzo, & Filosto, 2000).

Significant progress has been made in the prevention and management of many symptoms associated with cancer and its therapy. However, cancer-related anemia, which may affect more than half of all patients with cancer, often is assessed and treated inadequately. Severe anemia not only causes significant symptomology but also may impair functional status and quality of life. In addition, anemia has been found to affect treatment outcomes, including disease-free and overall survival. Therapeutic strategies, based on the underlying etiology of anemia, include iron supplementation, blood transfusion, and administration of recombinant human erythropoietin. Future approaches may involve novel agents under investigation that are designed to address current concerns related to efficacy, convenience, and possible cost-effectiveness of treatment of cancer-related anemia.

## Risk Factors and Prevalence

The prevalence of anemia in patients with cancer depends on diagnosis and stage of disease, type and timing of previous or current therapy, and concomitant conditions that could precipitate or intensify anemia (see Figure 1).

High rates of anemia have been observed in patients with lung cancer (52%) and ovarian cancer (51%). This may be because of the advanced ages of many patients with lung cancer, as well as the frequent use of platinum-based therapies to treat patients with these tumor types (Ludwig & Fritz, 1998). In a large audit of centers throughout the United Kingdom to assess the significance of anemia in patients with cancer, evaluation of 2,719 patients revealed that 33%—19% of patients with breast cancer and 43% of patients with lung cancer—required at least one blood transfusion (Barrett-Lee, Bailey, O'Brien, &

Wager, 2000). A review of the literature by Groopman and Itri (1999) similarly reported that the most significant anemia rates occur in patients with lung, gynecologic, and genitourinary tumors, with incidence ranging from 50%–60%.

Patients receiving myelosuppressive chemotherapy or radiation therapy are at risk for anemia as an accompanying toxicity. A low hemoglobin level ( $\leq 10$ – $12$  g/dL) at the initiation of cytotoxic chemotherapy also generally is considered a risk factor for development of anemia and need for subsequent blood transfusion (Thatcher, 1994). Using a hemoglobin level of less than 12 g/dL as the definition of functional anemia, Harrison, Shasha, White, and Ramdeen (2000) performed a random retrospective review of 202 patients with cancer receiving

radiation therapy. Of this group, 45% presented with functional anemia, and 57% eventually were anemic by the end of therapy.

Administration of platinum-based regimens also is correlated with an increased risk of anemia and need for transfusion support (Abels, Larholt, Krantz, & Bryant, 1996). Severe anemia, defined as grade 3–4 in the World Health Organization's and National

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