Hematopoietic hormones in the treatment of anemia related to cancer

Background
- This topic was initially selected in April 2004. The research questions identified during the topic refinement call held on November 18, 2004, were:
  - What is the cost-effectiveness of the using hematopoetic hormones in patients with cancer? In particular, evidence on the impact on the quality of life of cancer patients who do not receive chemotherapy as well as on the impact on chemotherapy dosing intensity (and overall survival) in cancer patients who experience chemotherapy-induced anemia would be of interest.
  - What is the evidence base supporting commonly used outcome/clinical target measures?:
    - What level of hemoglobin(Hg) is required for patients to start treatment? What is the appropriate Hg level to target? Is 120 g/L enough? Should treatment continue until 150 g/L? Is this valid for all disease states?
    - When should treatment with hematopoetic hormone be stopped?
    - Is measuring the baseline serum erythropoietin levels useful in initiating, monitoring treatment?

Disease Burden
- An estimated 153,100 new cases of cancer will be diagnosed in Canada in 2006.\(^1\) Approximately 30% of cancer patients develop anemia.\(^2\) Based on that, roughly 45,930 cancer patients per year could potentially be affected by increased availability of hematopoetic hormones.

Alternatives
- Standard care for anemia in cancer: blood transfusions (allogenic or autologous).
- Hematopoetic hormone options: i) erythropoietin, ii) darbepoeitin.

Clinical Impact
- Anemia is a common haematological abnormality encountered by cancer patients. It can be brought on by the cancer itself or by cancer therapy. Anemia usually leads to severe fatigue.\(^3\) Patients have reported that fatigue has a greater negative impact on their daily lives than many other cancer- or treatment-related complications. It has emotional and mental consequences including lack of self-motivation, sadness, frustration, and mental exhaustion. One survey found fatigue was considered so debilitating that 12% of patients felt their quality of life (QoL) was reduced to the point that they did not wish to continue living.\(^4\) Anemia is also an independent predictor of poor prognosis in cancer patients, as it is a risk factor for increased mortality. Treating anemia in cancer patients has the potential to improve their prognosis as well as QoL.\(^4\)
- Outcomes analyzed in studies on erythropoietin and darbepoeitin for cancer patients have included:
  - relative risk for blood transfusions and number of units transfused
Both transfusions and hematopoietic hormones can improve anemia. Recombinant erythropoietin is efficacious in reducing red blood cell transfusions and improving QoL in cancer patients. However, some conflicting results on survival have emerged. Two recent trials have reported patients on recombinant erythropoietin have fared worse than placebo with respect to progression-free survival. A recent Cochrane review concluded the effect on tumour response and overall survival remains uncertain. The Cochrane review authors also advised caution when using epoetin or darbepoetin in combination with thrombogenic chemotherapeutic agents or for cancer patients who are at high risk for thrombo-embolic events. A recent meta-analysis of three Canadian trials, as well as a US review, concluded that early erythropoietic treatment (when anemia is relatively mild) can optimize clinical benefit in cancer patients receiving chemotherapy. Another Canadian study found that transfusions prior to epoetin alpha therapy increase the risk of future transfusions, and early treatment with epoetin alfa might reduce the risk of subsequent transfusions.

**Budget Impact**

- Assuming all cancer patients developing anemia would receive a three month treatment with a hematopoietic hormone (erythropoietin), the net additional drug cost in Canada would be about C$ 313 million [US$3700 in 1998 converted to 2006 C$] x 45,930 patients].
- Costs for darbepoetin and epoetin appear to be similar, although differences in costs have been reported either in favour of darbepoetin or in favour of erythropoietin.

**Economic Impact**

- Economic benefits from treatment with hematopoetic hormones include reductions in direct costs due to blood transfusion and treatment of related complications. They may also include a positive effect on QoL, although such benefits are not well reflected in many economic evaluations and budget impact analyses.

- Not all patients with cancer respond to hematopoietic hormone treatment, so cost-effectiveness could be improved by identifying those patients who are more likely to respond. Some evidence suggests recombinant human erythropoietin may be more effective for patients experiencing chemotherapy-associated anemia than those with “anemia of cancer”. It is possible that economic benefits include a reduction in indirect costs associated with positive effect on productivity since studies have found that reductions in anemia and fatigue are associated with improvements in productivity in cancer patients receiving chemotherapy.
Evidence

- A comprehensive health technology assessment on this topic by NICE in the UK is expected to be released in January 2007.\textsuperscript{29} It will include a synthesis of clinical evidence and an economic evaluation.

- The literature search found several economic evaluations.\textsuperscript{17,18,21,23,30-35} One was a Canadian cost-benefit study taking a health care system perspective.\textsuperscript{15} It is referred to above in the budget impact section, and included a survey of the general Canadian public on their willingness-to-pay to use epoetin alpha.

- The literature search found several reviews of clinical evidence and meta-analyses.\textsuperscript{6,8,10-13,16,24,36-47} As well, a Cochrane review is currently in progress on the treatment of head and neck cancer, to review RCTs comparing the effectiveness of erythropoietin plus radiotherapy versus radiation alone.\textsuperscript{48}

- The literature search also found some relevant practice guidelines and related articles,\textsuperscript{3,23,49-52} including guidelines developed for Cancer Care Ontario on erythropoietin in management of cancer patients with non-hematologic malignancies receiving chemotherapy.\textsuperscript{53}

References


