patients as anemic or nonanemic and then using these labels to design interventions. There is a more subjective aspect of anemia that is somewhat similar to pain in that the patient is the one perceiving and reporting associated problems, and the symptoms may or may not be classic signs of anemia occurring at some established Hgb cut-off point. Thus, it is important to continually assess patients and hear about their symptoms, in addition to looking at laboratory values and associated trends over time. An asymptomatic patient with an Hgb of 9 g/dL may benefit greatly from EST, but another patient who is at 10.5 g/dL and symptomatic also may derive significant benefit.

JHAS/iN: In clinical studies, darbepoetin alfa has shown efficacy at an every-3-week dosing schedule versus a weekly or 3 times weekly dosing schedule of epoetin alfa. How does this compare in terms of cost and cost-effectiveness?

Dr Gillespie: Very few studies have investigated the cost of anemia and the cost-effectiveness of its therapies, much less compared the cost-effectiveness among different interventions. Several studies found that anemia significantly increases healthcare costs, both directly and indirectly.6,7 Nissenson et al reported that medical costs for patients with cancer who have anemia can be as much as twice those for patients with cancer who are not anemic.8 However, other findings suggest that patients with anemia who are treated with EST experience similar costs to those patients without anemia.9

JHAS/iN: How are you using these agents in your clinical practice?

Dr Gillespie: Because my practice encompasses a university medical center and a Veterans Affairs (VA) medical center, some of our protocols may differ from what is commonly done in community settings. At the Atlanta VA Medical Center, some of our patients may already be anemic at the time of cancer diagnosis, as a result of the cancer itself, the stage at which it is diagnosed, prior nutritional deficits, or lifestyle issues. These patients are not only at risk for anemia because of chemotherapy, but also may begin treatment with significant anemia and require interventions to address their anemia even
before initiating chemotherapy. For other patients, especially elderly patients, we may use risk models to assist with risk assessment. In my practice, we are focused particularly on the special needs of older patients and are fairly aggressive in intervening when anemia is still mild to moderate to prevent it from progressing to a severe phase.

**JHAS/N: Is it possible to improve economic efficiency without compromising quality-of-care and detracting from optimal patient outcomes?**

*Dr Gillespie:* To conduct a valid economic analysis, direct medical costs, such as drugs and treatments, and indirect costs, including patient-reported outcomes (eg, health-related QOL) and economic factors (eg, lost productivity or medical leave from work), should be examined. Studies examining the cost-effectiveness of EST, especially when compared to transfusion therapy, are historically difficult to conduct and analyze. Theoretically, it should be possible to incorporate the QOL and indirect cost measures with the more direct measures, enabling a patient to achieve good QOL and outcomes while maintaining economic efficiency.

**JHAS/N: How does anemia compromise chemotherapy dosing schedules?**

*Dr Gillespie:* Anemia can interfere with the optimal dose and the optimal schedule for chemotherapy. Age, certain chemotherapeutic agents, bone marrow involvement, prior therapy, renal function, and preexisting anemia are all factors that can help predict whether patients are at greater risk for compromising the prescribed dose and schedule of their chemotherapy. In addition, we know that certain therapies, including radiation and other agents, rely on oxygenation for their delivery, and anemia can interfere with treatment efficacy as a result. We also have learned that hypoxia is a trigger for metastatic disease; therefore, avoiding hypoxia by preventing or treating anemia may actually impact the process of metastasis.

**JHAS/N: How can oncology APNs and oncology PAs avoid chemotherapy dose delays and dose reductions in patients with anemia?**

*Dr Gillespie:* First, by being proactive rather than reactive for management of all symptoms, including anemia. Because of the long lead-in period before EST is effective, we cannot afford to wait until anemia is already severe and then be reactive to that significant condition. Second, oncology APNs and oncology PAs are often the primary healthcare providers to assess patients for their history, prior therapies, nutritional status, stage of disease, and other factors that may indicate an increased risk for or already contribute to an existing anemia. Third, they usually oversee patients' laboratory values on a regular basis and are in a prime position not only to note when significant anemia occurs, but also to note trends toward trouble in that direction. Fourth, oncology APNs and oncology PAs may be the key healthcare providers to ensure compliance with guidelines for optimal management of anemia in their practice, or they may be essential in implementation of anemia treatment if such guidelines are not already in place.

**JHAS/N: What effect does erythropoietic intervention have on cancer therapy outcomes?**

*Dr Gillespie:* Several studies report the effect of erythropoietic interventions on important clinical outcomes. It has been well-documented that EST results in increases in Hgb, decreases in transfusion requirements, and improvements in QOL. However, a large European study of more than 15,000 patients with cancer also found that anemia was an independent predictor of poor prognosis. In a systematic review, a 65% overall increase in risk of mortality was found in patients with cancer who have anemia. Similarly, an analysis of 19 clinical studies of anemia and 8 studies of tumor hypoxemia demonstrated a strong association between low Hgb and/or higher levels of tumor hypoxia with poorer prognosis. Whereas some recent studies have reported mixed results from EST, and even a decrease in survival correlated with erythropoietic interventions, these studies had significant methodological flaws. More research is needed to make definitive statements regarding the impact of anemia or EST on clinical outcomes, such as survival, but their roles related to other outcomes (ie, Hgb, transfusions, or QOL) are much clearer.

**REFERENCES**