

# The Impact of a Long-Acting Erythropoiesis Stimulating Protein on Patient Throughput in a Hospital-Based Ambulatory Oncology Clinic

Niesha Griffith, MS, RPh,\* Colleen Allen, RN, MBA,<sup>†</sup> Andrew Pultz, RPh, PharmD,<sup>‡</sup> and Sam Penza, MD<sup>§</sup>

## ABSTRACT

**Objectives:** To quantify labor and time expended, resources used, and the net impact on patient throughput and staff time (from the institution's perspective) associated with short-acting (epoetin alfa) and long-acting (darbepoetin alfa) erythropoietin stimulating proteins (ESPs).

**Design:** Prospective time/motion assessment and retrospective chart review of patient visits and resources used.

**Setting:** Single hospital-based ambulatory oncology clinic.

**Methods:** Time and motion measurements related to patient treatment and drug preparation were collected for (1) patient check-in; (2) phlebotomy; (3) laboratory processing; (4) pharmacist assessment/counseling; and (5) ESP preparation, administration, and documentation. ESP use for 266 chemotherapy cycles administered between August 1, 2003 and March 31, 2004 was grouped as epoetin alfa only and darbepoetin alfa only.

**Results:** For 313 observed events, the mean total time calculated for the 5 prespecified activities associated with a visit for ESP administration was 55.4 minutes, of which pharmacy assessment/counseling was responsible for the majority of time expended (22.6 min). A significant (23%) reduction in the number of mean visits per cycle was recorded for the darbepoetin alfa group ( $P < 0.001$ , resulting in 1 less visit per average chemotherapy cycle). This difference remained statistically different (42% reduction;  $P < 0.001$ ) when the mean number of visits specifically for ESP administration was compared between the darbepoetin alfa and epoetin alfa groups. Darbepoetin alfa recipients also received significantly fewer doses of ESP per cycle compared with those given epoetin alfa ( $P < 0.001$ ). The use of darbepoetin alfa saved the clinic 125 hours of staff/patient time per cycle with a potential of 120 hours/cycle additional savings if the epoetin alfa patients had received this long-acting ESP. During calendar year 2004, 610 patients received a red-cell growth factor following chemotherapy for a solid tumor. These patients represent an average of 3,660 cycles of chemotherapy per year. The reduction in visits (1/cycle) with long-acting ESP, at 55.4 minutes of staff time per visit, will potentially result in avoidance of 3,379.4 hours of staff time or 1.62 full-time equivalents per year.

**Conclusions:** Patient office visits for ESP administration are associated with significant time for clinic staff. A long-acting ESP, such as darbepoetin alfa, may enable significant time savings for clinic staff and providers by reducing the number of necessary visits for ESP administration. The time saved also provides an opportunity to reallocate staff to perform additional supportive care activities.

**Keywords** — anemia; erythropoiesis stimulating protein; ESP; practice dynamics; practice efficiency; throughput; oncology; outpatient; resource utilization; epoetin alfa; darbepoetin alfa

Hosp Pharm — 2008;43:388-395

## NOTE

*This work was conducted, and the manuscript was drafted, prior to safety issues raised regarding ESPs in*

*early 2007. The reader should keep this in mind when reviewing this article. The authors continue to feel strongly that the issues raised con-*

*cerning workload are very real for typical clinic operations in hospitals today. We also continue to believe that the improvement of patients'*

\*Director of Pharmacy, Arthur G. James Cancer Hospital, Ohio State University, Columbus, Ohio, Associate Director of Pharmacy, The Ohio State University Medical Center, Clinical Assistant Professor, Division of Pharmacy Practice and Administration, The Ohio State University College of Pharmacy; <sup>†</sup>Director of Performance Improvement and Patient Safety, Northern Michigan Regional Health System, Petoskey, Michigan, at the time of this study she was Director, Clinical Quality and Resource Management, Arthur G. James Cancer Hospital, Ohio State University; <sup>‡</sup>Outpatient Oncology Pharmacist, Arthur G. James Cancer Hospital, Ohio State University, Columbus, Ohio; <sup>§</sup>Medical Director, Outpatient Services, Arthur G. James Cancer Hospital, The Ohio State University, Associate Professor of Clinical Medicine, Ohio State University College of Medicine.

*quality of life and ability to perform daily activities (work, child rearing, etc) is as important an issue as ever. We look forward to seeing studies conducted that are designed to confirm or clarify the recent safety issues regarding ESP use in cancer patients.*

While national rates of newly diagnosed cancers and death rates appear to be stabilizing as of the mid-1990s,<sup>1</sup> anemia induced by chemotherapy (chemo) and radiation therapy continues to greatly diminish patient quality of life, creating significant patient inconvenience, morbidity, and the need for ongoing supportive care from health care providers. Fortunately, the management of many chemo-related adverse effects, including anemia, has dramatically improved. The availability of recombinant erythropoietin stimulating proteins (ESPs; also known as ESAs) aimed at reducing the morbidity and mortality associated with chemo- and malignancy-induced anemia represents a major advancement in the last decade.<sup>2,3</sup>

The prevalence of anemia is high (ie, 35% to 95%) in patients with cancer, whether or not they are actively receiving chemo and/or radiation therapy.<sup>4-6</sup> Cancer-related anemia is the cause of many debilitating symptoms. Fatigue, although a multifactorial phenomenon in cancer patients, is often associated with anemia and may be the most distressing of these symptoms. The multidisciplinary Fatigue Coalition claims that two-thirds of patients with cancer experience fatigue, often on a daily basis.<sup>7-9</sup> As such, effected patients typically experience a reduced ability to perform normal daily functions (eg, work, social, recreational, and day-to-day activities). Anemia is also associated with reduced

health outcomes, in part because of reduced compliance with the prescribed treatment regimen, subsequently leading to a lower quality of life.<sup>10-14</sup> The economic impact of fatigue to the patient and his or her family can be significant (eg, reduced overall work hours, increased caregiver time off from work).<sup>15</sup>

Two medication treatment options are currently available for the treatment of anemia associated with chemotherapy in patients with nonmyeloid malignancies: epoetin alfa (*Procrit*; Ortho Biotech, Raritan, NJ) and darbepoetin alfa (*Aranesp*; Amgen, Thousand Oaks, CA). Epoetin alfa is usually administered as a weekly subcutaneous injection, starting at 40,000 units/dose. Two previous studies have established that epoetin alfa improves the quality of life in patients receiving chemotherapy, likely secondary to increased hemoglobin (Hgb) levels, regardless of tumor type or response.<sup>16,17</sup> Darbepoetin alfa, a modified recombinant form of erythropoietin, has a 3-fold longer half-life compared with epoetin alfa in patients with cancer.<sup>18</sup> Accordingly, darbepoetin alfa can be administered less frequently and has shown to be clinically effective in increasing Hgb levels and improving patient quality of life.<sup>18-27</sup>

The current era of cost consciousness demands that the selection of the optimal chemo-treatment regimen, including the need for adjuvant therapies, is safe and effective for the patient as well as cost effective for the institution; this includes consideration of both direct and indirect costs to the institution. Epoetin alfa has been used in patients with cancer for more than a decade. However, this relatively short-acting ESP requires multiple injections that necessitate

multiple visits by patients to an oncology clinic during each chemo cycle, solely for the administration of ESP and evaluation of complete blood cell count (CBC). In addition to the inconvenience for patients and their caregivers, frequent clinic visits for ESP administration require time and effort on the part of the health care providers. The advent of a long-acting ESP, darbepoetin alfa, may improve patient satisfaction and positively impact patient throughput (number of patients seen in the clinic per day) in the ambulatory setting.

Consideration of cost savings to the institution has recently taken on a new meaning. In the past, a cost-effective agent was simply evaluated based on a drug's acquisition cost, preparation and administration fees, and necessary laboratory monitoring costs. Today, other factors including medication dosing schedules, frequency of clinic visits, time for patient scheduling, record-keeping, and billing all represent cost considerations to the institution. Reducing these factors may indeed provide the most cost-effective therapy for an institution. For example, a longer-acting agent can be administered less often and requires less monitoring, thus freeing up clinic space with patient-visit and staff-time reductions. The clinic's free space and available staff time may be more effectively reallocated to other patient needs (eg, initial cancer evaluation and work-up, administration of chemo rather than ESP and/or CBC monitoring) with the potential for increased revenue generation.

Based on the need to improve adherence to prescribed anemia-management regimens, the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute at The Ohio State University (hereafter referred to as the James

Cancer Center) has developed an innovative pharmacy-initiated program—the Anemia Management Program (AMP)—to facilitate and improve the care of its oncology patients. This multidisciplinary health care program is aimed at promoting the appropriate use of ESPs for anemia. Patient education is a key component of the program to ensure that injections are received on time and target Hgb levels are achieved and maintained. Once patients in need of erythropoietic support are identified, the physician or nurse practitioner orders the ESP indicating “pharmacy to dose.” Pharmacists determine the appropriate initiating dose, order laboratory tests (eg, iron studies, CBC), and educate the patient, based on a medical staff approved medication-use guideline. At the time of this study, both ESPs were on the formulary at the James Cancer Center for use in patients undergoing chemo (in accordance with National Comprehensive Cancer Network Practice Guidelines for Oncology: Cancer- and Treatment-Related Anemia for ESP use).<sup>28</sup> Selection of the product was left to the discretion of the prescriber, as both products were considered comparable in terms of efficacy and safety.

Similar to most hospital-based outpatient oncology clinics, the James Cancer Center outpatient clinics are experiencing a rapid growth in the demand for their services. As such, opportunities to improve throughput, related to both medications and services provided, must be continually evaluated. In an effort to evaluate the opportunities associated with the management of ESPs in the outpatient clinics, a trial was undertaken to assess the impact of using a short-acting versus long-acting ESP on clinic throughput. The trial

employed a design and methodology similar to that of a previously published trial conducted in the private practice sector.<sup>22</sup> The first objective was to record and time all health care events (time and motion assessments) involved with a single patient visit for ESP injection (ie, epoetin alfa, darbepoetin alfa) in adults who were receiving chemo for solid tumors. A second objective of the trial was to retrospectively determine the number of ESP visits required per single cycle of chemo stratified by those patients receiving epoetin alfa or darbepoetin alfa. A third objective was to determine staff resources and time that could be saved or reallocated to other patient care activities. The overall goal of the study was to determine if darbepoetin alfa reduced the number of clinic visits, thus saving practice time and expense.

## **METHODS**

A 2-phase, 4-week study was conducted at a hospital-based ambulatory oncology clinic at the James Cancer Center. The study design was approved by the institutional review board. The time and motion analysis and chart-review criteria were identical to those used in the previously published study in the private practice setting.<sup>21</sup>

### **Time and Motion Assessments**

Time and motion measurements for various aspects of an ESP visit were conducted during weeks 1 and 2 by two trained nurses through observation of clinic activities. The amount of time to conduct each of the 5 separate and distinct events was measured and recorded on standardized case report forms: patient check-in, phlebotomy, laboratory processing, pharmacy assessment and

counseling, and ESP preparation/administration/documentation. Time measurements began and ended based on predefined steps within each event. These steps were identified from prior observations of these activities in the clinic. The study observations included a mix of new and existing patients in an effort to capture the average amount of time spent on each event. A total of 60 measurements for each of the 5 aforementioned events were sought.

### **ESP Utilization**

A retrospective chart review of ESP use for a single chemo cycle was conducted and patients were grouped into 2 categories: patients who received epoetin alfa only and patients who received darbepoetin alfa only. Patient records were reviewed consecutively in reverse chronological order from August 1, 2003 through March 31, 2004 for patients who had their chemo cycle started and completed during the August 1, 2003 through March 31, 2004 interval. More than 1 eligible cycle was allowed per patient.

Every record for each ESP category was flagged and reviewed for the following inclusion criteria: men and women 18 years of age or older who were receiving chemo for solid tumor types, including lymphoma; had chemo cycles of 14 to 28 days; received at least 1 dose of epoetin alfa or darbepoetin alfa during the cycle; and had complete documentation of ESP administration and laboratory testing data for the reviewed cycle. Day 0 of a cycle was considered the day chemo was started and the last day of the cycle was the day prior to the next scheduled chemo dose or when 28 days elapsed. Records were excluded if patient data revealed any of the following: self-administration of either ESP, receipt of a granulocyte

**Table 1. Time/Motion Measurements of Erythropoiesis Stimulating Protein (ESP) Related Tasks**

<i>Event</i>	<i>N</i>	<i>Mean Staff Time (min)</i> <i>(standard deviation)</i>	<i>95% CI</i>
Patient Check-In	65	3.7 (2.6)	3 to 4.3
Phlebotomy	63	10.3 (6.7)	8.6 to 12
Laboratory Processing	57	12.9 (9.7)	10.3 to 15.5
Pharmacist Assessment/Counseling	61	22.6 (13.4)	19.2 to 26.1
ESP Preparation, Administration and Documentation (All)	67	5.9 (4.5)	4.8 to 7
<b>Total Process Time/Visit</b>		<b>55.4 min</b>	

CI = confidence interval

**Table 2. Demographics – Chart Review Erythropoiesis Stimulating Protein Patients**

	<i>Epoetin Alfa</i>	<i>Darbepoetin Alfa</i>
Total Cycles	130	136
Patient Age (Years)		
Mean	61	61
Range	53 to 71	57 to 66
Female	66	95
Male	64	41

cyte or granulocyte-macrophage colony stimulating factor, or receipt of both epoetin alfa and darbepoetin alfa during the same cycle.

From each chart of eligible patients, baseline demographic data were collected (ie, age, gender). Therapy-specific data were also recorded including: days in cycle of doses of all chemo agents given, day of first chemo (if any) of next cycle, days in cycle of doses of all epoetin alfa or darbepoetin alfa doses administered, and days in cycle of all CBCs. The primary end point was the total number of visits per cycle devoted to 3 interventions: chemo administration, CBC determinations, and ESP administration. A secondary end point was the number of visits per cycle for ESP administration.

**Statistical Analysis**

Clinic staff time required for each time and motion component of a visit was summarized by the mean, standard deviation and 95% confidence intervals. Chart review data were summarized on a per-cycle basis. Fisher exact or chi-square tests were used to detect any significant differences in baseline characteristics. Other than observing a larger percentage of females in the darbepoetin (see Results), no imbalances in baseline characteristics were evident, therefore, the number of visits per cycle was compared using the Student *t* test.

**RESULTS**

**Time and Motion Assessments**

A total of 313 events were subjected to standard time and motion

observations and measurement. The breakdown of the time expended for each of the 5 events measured is depicted in Table 1. The sum of all 5 average times resulted in a mean of 55.4 minutes of staff time consumed by a single typical clinic visit for ESP administration. The majority of time was spent on pharmacy assessment/counseling (mean 22.6 min; standard deviation 13.4 min), followed by laboratory processing (mean 12.9 min; standard deviation 9.7 min), and phlebotomy procedures (mean 10.3 min; standard deviation 6.7 min). It is important to emphasize that the total clinic staff time expended for ESP administration for each patient does not include any other time spent between each of the 5 events, such as discussing issues with staff, additional counseling of patients and family by other health care staff, or time spent with scheduling additional appointments.

**ESP Utilization**

A total of 130 chemo cycles (representing 64 patients) in the epoetin alfa group and 136 chemo cycles (representing 66 patients) in the darbepoetin alfa group were retrospectively reviewed. The mean age of the patients was 61 years in each of the ESP groups (see Table 2). In the epoetin alfa group, a similar number of men and women were evaluated (66 vs 64, respectively). However, in the darbepoetin alfa group, more than twice as many women received this ESP compared with men (95 vs 41, respectively). This difference is a result of the breast cancer specialists being early adopters of darbepoetin due to its extended dosing. The average cycle length was nearly identical in each of the ESP groups (23 vs 22 days; see Table 3).

Based on the 266 reviewed

**Table 3. Mean Erythropoiesis Stimulating Protein (ESP) Visits and Utilization Per Cycle**

	<i>Epoetin Alfa</i>	<i>Darbepoetin Alfa</i>	<i>P value</i>
Sample Size	130 cycles	136 cycles	
Average Cycle Length	23 days	22 days	
<b>Visits</b>			
All visits <sup>a</sup>			
Mean (standard deviation)	4.4 (1.9)	3.4 (1.5)	< 0.001
Chemotherapy visits <sup>b</sup>			
Mean (standard deviation)	2.4 (1.3)	2 (1)	< 0.01
ESP visits <sup>c</sup>			
Mean (standard deviation)	1.2 (1.0)	0.7 (0.6)	< 0.001
CBC only visits <sup>d</sup>			
Mean (standard deviation)	0.8 (1.3)	0.8 (1.2)	< 0.63
<b>Laboratory</b>			
CBCs obtained			
Mean (standard deviation)	3.8 (1.6)	3 (1.4)	< 0.001
<b>ESP</b>			
Doses administered			
Mean (standard deviation)	2.6 (0.9)	1.6 (0.6)	< 0.001

CBC = complete blood cell count; <sup>a</sup>Any visit at which either chemotherapy or ESP was given, or CBC was obtained; <sup>b</sup>Visit at which chemotherapy was given (may also include CBC or ESP); <sup>c</sup>Visit at which ESP was administered; chemotherapy not given; <sup>d</sup>Visit at which neither chemotherapy nor ESP was given but CBC was obtained.

cycles, a total of 332 epoetin alfa and 215 darbepoetin alfa doses were recorded. The most frequent dose of epoetin alfa was 40,000 units (46%) followed by 60,000 units (37%). The most prevalent dose of darbepoetin alfa was 200 mcg (46%) followed by 300 mcg (37%).

Patients given epoetin alfa had an average of 4.4 clinic visits per cycle for any reason compared with darbepoetin alfa recipients who had a mean of 3.4 visits per cycle (see Table 3). Accordingly, patients given darbepoetin alfa had a significant 23% (1 visit) reduction in the mean number of total visits per cycle compared with the epoetin alfa group ( $P < 0.001$ ). The number of mean visits specifically

for ESP administration was reduced by 0.5 visits per cycle (42% reduction) when darbepoetin alfa was the ESP administered ( $P < 0.001$ ). This difference also corresponds with the 38% reduction in the number of doses of darbepoetin administered per cycle compared with epoetin alfa (1.6 vs 2.6 per cycle;  $P < 0.001$ ). The average number of doses per cycle also corresponds with a 3-week cycle length when dosed every week for epoetin alfa and every other week for darbepoetin alfa. No difference was observed in the mean number of visits for CBC determination only, between the 2 ESP groups (each mean of 0.8 visits). However, the darbepoetin alfa group had an average of 0.8 fewer blood draws

per cycle for CBCs compared with the epoetin alfa group ( $P < 0.001$ ).

Overall, the 136 cycles of darbepoetin alfa administered resulted in greater efficiency for the James Cancer Center by reducing the number of patient visits. The total of 136 visits in the darbepoetin alfa group resulted in an avoidance of 125 hours of staff and patient time for ESP management (ie, the product of 136 cycles and 55 min avoided/visit). If patients who received epoetin alfa in the remaining 130 cycles were converted to darbepoetin alfa, an additional 120 hour avoidance could have been realized, for a total avoidance of 245 hours of staff time and patient time.

**DISCUSSION**

For the last 2 decades, there has been mounting pressure upon the health care industry to minimize costs and increase revenue generation, while continuing to provide quality patient care in the face of increasing demand. Accordingly, clinicians now strive to evaluate and treat patients in a more efficient manner and, when possible, limit the use of unnecessary diagnostic tests, surgeries, and expensive medications. Current economic pressures are further compounded secondary to advances in medicine, which have created a larger pool of patients who require chronic care. For example, the management of patients with hematologic or solid-tumor malignancies demands frequent medical visits, both inpatient and outpatient, for a variety of interventions. In many sectors of medicine, including oncology, patients are routinely waiting to be seen for initial/follow-up evaluation to receive chemo or ancillary therapies and/or for toxicity monitoring. Physicians, hospitals, and

clinics are struggling to provide optimal and timely care to all who need it, while attempting to reduce health care costs. Maximizing throughput becomes increasingly important in the face of these challenges.

Central to meeting the extremely high demand for clinical services, the James Cancer Center (66% projected growth over 3 years), which is one of the nation's 39 designated National Cancer Institute (NCI) Comprehensive Cancer Centers, is currently comprised of 4 outpatient oncology clinics—the fourth clinic was opened in August of 2004. The finite volume of clinic capacity often proves challenging for both patients attempting to access the center and to the providers attempting to optimize their patient's management. This is evident by the fact that the most recent ambulatory site brought on line was meeting preliminary 6-month volume projections less than 2 months after opening.

Given that all physicians at the James Cancer Center are scientist clinicians, they are afforded the opportunity to provide "focused care" to specific categories of patients of professional interest (eg, breast, prostate, or lung cancer patients). However, their professional research time, by design, is protected to allow for scientific research and inquiry. Physician time in the clinic may range from 1 day every other week to 3 days per week. As such, clinic administrators are striving to identify means to increase clinic throughput by refocusing physician clinical time on core therapeutic interventions for selected patients, while managing supportive and ancillary care provided through midlevel providers, advance-practice nurse clinicians, and clinical pharmacists.

The first objective of this study was to calculate clinic staff time associated with the administration of a short- and long-acting ESP to patients receiving chemo for solid tumors. Administration of a single-ESP injection (either epoetin alfa or darbepoetin alfa, respectively) in this large, hospital-based oncology clinic consumed approximately 1 hour of staff time per patient visit. Notably, patient assessment/counseling by the pharmacist consumed approximately 20 minutes or one-third of the time expended per ESP visit. A subsequent retrospective analysis of 266 chemo cycles found that patients given darbepoetin alfa required 1 less clinic visit per cycle (a 23% reduction) compared with those who received epoetin alfa ( $P < 0.001$ ). Darbepoetin-treated patients also had significantly fewer clinic visits solely for the purpose of ESP administration (ie, 0.5 fewer visits per cycle [42% reduction]) compared with epoetin alfa recipients ( $P < 0.001$ ). Additionally, there was a significant reduction (38%) in the number of doses of darbepoetin alfa administered per cycle compared with epoetin alfa ( $P < 0.001$ ).

During calendar year 2004 (January 1 to December 31), 1,162 patients with solid tumors received chemo for their disease at the James Cancer Center. Of those solid-tumor patients, 610 (52.5%) received an ESP during their chemo. Assuming an average of 6 cycles of chemo per patient, 610 patients represent 3,660 cycles of chemo per year. Had the entire cohort of patients received epoetin only, conversion of the entire cohort to a long-acting ESP would result in a reduction of 3,660 visits. At 55.4 minutes of staff time per visit, the resultant staff time reduction would be 3,379.4 hours or 1.62 full-time equivalents per year.

Reduction in staff times could also be represented as dollars saved. However, in the majority of instances, it is unlikely that staff positions would be eliminated, resulting in actual dollars saved. Rather, it is more likely that the realized time savings would be "reallocated" or "transferred" to other patient care activities. As this study was conducted prior to the FDA approval of every 3-week dosing for darbepoetin alfa, a further reduction in ESP administration visits, and increase in staff time saved may be expected.

This study evaluated isolated chemo cycles rather than complete patient regimens, primarily due to time and procedural constraints. A more definitive analysis might include all cycles for each individual patient during a complete chemo regimen for both the time/motion and ESP utilization portions of the study. This is being considered in a future evaluation.

These data are important to the physician/staff, the patient, and the institution for a number of reasons. The ability of the long-acting ESP, darbepoetin alfa, to reduce staff time by approximately 1 hour per patient per cycle potentially permits staff to provide care to other patients for initial follow-up evaluation, chemo, and other related needs. Accordingly, these data demonstrate that darbepoetin alfa frees up clinic space and staff time, thereby increasing clinic throughput and capacity. The use of any medication that can be given less often and requires fewer monitoring visits may improve patient satisfaction and quality of life. Indirectly, use of darbepoetin alfa may benefit other patients in an oncology clinic as there will be less delay in their ability to receive evaluation and treatment. The opportunity to reallocate staff may increase

patient throughput as well as allow for additional involvement in other collaborative supportive care programs (eg, antiemetic management, neutropenia risk assessment).

The findings of the current study correlate with the previous trial conducted in 2 large-private oncology practices that also included an evaluation of time and motion measurements and ESP utilization.<sup>22</sup> In the former study, long-acting growth factors directed at both anemia and neutropenia (ie, pegfilgrastim plus darbepoetin alfa) resulted in significant time savings for physicians/staff by reducing the number of necessary office visits for drug administration. Somewhat different from the James Cancer Center experience reported herein, the previous study estimated that each ESP administration was associated with a mean total clinic staff time of 22.1 minutes (a third of that observed in the current trial).<sup>22</sup> The main reason for time difference observed in the 2 studies is that pharmacists were not integral to the process in the private practice setting. Certainly, size and complexity of an academic medical center compared to a private oncology practice was a contributing factor but the time spent by pharmacists assessing and counseling patients and ensuring appropriate use of ESPs stands out in the comparison.

Nonetheless, for the cohort that received only epoetin alfa or darbepoetin alfa in the previous trial, use of darbepoetin resulted in a 48% reduction ( $P < 0.01$ ) in mean number of doses administered per cycle, although the use of darbepoetin alfa only saved the clinic staff/providers 0.1 hours and saved patients 0.4 hours per chemo cycle.<sup>22</sup> The authors hypothesized that this lack of significant time difference was attributable to the

fact that patients were still brought into the office weekly for CBC determination, even though they were receiving darbepoetin alfa. This underscores the need for staff education whenever a long-acting agent is introduced in order to maximize the benefit of less frequent dosing and fewer required visits.

The effort to quantify the highly complex econometric impact on overall capacity at the James Cancer Center continues in earnest outside the initial results of this study. Going forth, the hypothesis that is held by administration is that increasing the number of functional clinical pipelines, where patients can receive treatment on a stratified basis, will allow an optimal utilization of the most rate-limiting resource in the system (ie, number of physicians with specialized focus). A number of initiatives are being explored to focus the institution's medical-intellectual capital on core missions of research, teaching, and clinical care. This is evidenced by the pharmacy's AMP, which uses medical staff-approved guidelines for the management of ESPs, thus appropriately freeing physician time away from direct supportive care intervention, toward primary therapeutic interventions. By dedicating resources to the long-term monitoring and management, the AMP endeavors to ensure appropriate use of expensive medications, minimize the negative impact of anemia on the prescribed chemo schedule and unscheduled use of provider resources, ensure maximum therapeutic benefits for patients, and improve patient satisfaction.<sup>29</sup> With the recent addition of a black box warning, there is a heightened concern for patient safety with the use of ESPs and therefore a greater importance

being placed on the appropriate monitoring of these patients. Now more than ever, pharmacists can play a key role in ensuring safe and cost effective use of these medications. A study evaluating the impact of the AMP on guideline adherence<sup>30</sup> and patient outcomes is currently underway.

The use of growth factors to combat anemia and neutropenia has escalated in recent years. The choice of which ESP to use is governed by many factors, including economic considerations and the need to improve patient quality of life. Institutions and patients are attempting to streamline and/or avoid health care associated costs. Selection of a medication or treatment, which may save time for physicians/clinic staff, enhance clinic throughput, and improve a patient's quality of life should be carefully considered. Although cost will always be a factor, basing a decision entirely on the acquisition cost of one medication versus another is no longer prudent in this current complex and challenging health care environment.

#### **ACKNOWLEDGEMENT**

The authors would like to thank RJM Group, LLC for their assistance and support in carrying out this study.

#### **REFERENCES**

1. Weir HK, Thun MJ, Hankey BF, et al. Annual report to the nation on the status of cancer, 1975-2000, featuring the uses of surveillance data for cancer prevention and control. *J Natl Cancer Inst.* 2003;95(17):1276-1299.
2. Crawford J, Cella D, Cleeland CS, et al. Relationship between changes in hemoglobin level and quality of life during chemotherapy in anemic cancer patients receiving epoetin alfa therapy. *Cancer.* 2002;95(4):888-895.
3. Mock V, Atkinson A, Barsevick A, et al. National Comprehensive Cancer Net-

- work. NCCN Practice Guidelines for Cancer-Related Fatigue. *Oncology* (Williston Park). 2000;14(11A):151-161.
4. Bron D, Meuleman N, Mascaux C. Biological basis of anemia. *Semin Oncol*. 2001;28(2 suppl 8):1-6.
  5. Groopman JE, Itri LM. Chemotherapy-induced anemia in adults: incidence and treatment. *J Natl Cancer Inst*. 1999;91(19):1616-1634.
  6. Harrison LB, Sasha D, White C, Ramdeen B. Radiotherapy associated anemia: the scope of the problem. *Oncologist*. 2000;5(suppl 2):1-7.
  7. Curt GA. The impact of fatigue on patients with cancer: overview of FATIGUE 1 and 2. *Oncologist*. 2000;5(suppl 2):9-12.
  8. Curt GA, Breitbart W, Cella D, et al. Impact of cancer-related fatigue on the lives of patients: new findings from the fatigue coalition. *Oncologist*. 2000;5(5):353-360.
  9. Vogelzang NJ, Breitbart W, Cella D, et al. Patient, caregiver, and oncologist perceptions of cancer-related fatigue: results of a tripart assessment survey. The Fatigue Coalition. *Semin Hematol*. 1997;34(3 suppl 2):4-12.
  10. Caro JJ, Salas M, Ward A, Goss G. Anemia as an independent prognostic factor for survival in patients with cancer: a systemic, quantitative review. *Cancer*. 2001;91(12):2214-2221.
  11. Fein DA, Lee WR, Hanlon AL, et al. Pretreatment hemoglobin level influences local control and survival of T1-T2 squamous cell carcinomas of the glottic larynx. *J Clin Oncol*. 1995;13(8):2077-2083.
  12. Lee WR, Berkey B, Marcial V, et al. Anemia is associated with decreased survival and increased locoregional failure in patients with locally advanced head and neck carcinoma: a secondary analysis of RTOG 85-27. *Int J Radiat Oncol Biol Phys*. 1998;42(5):1069-1075.
  13. Littlewood TJ, Bajetta E, Nortier JW, Vercammen E, Rapoport B, for the Epoetin alfa Study Group. Effects of epoetin alfa on hematologic parameters and quality of life in cancer patients receiving nonplatinum chemotherapy: results of a randomized, double-blind, placebo-controlled trial. *J Clin Oncol*. 2001;19(11):2865-2874.
  14. Tchekmedyan NS, Hickman M, Siau J, Greco A, Aisner J. Treatment of cancer anorexia with megestrol acetate: impact on quality of life. *Oncology* (Williston Park). 1990;4(5):185-192, 194.
  15. Lyman GH, Berndt ER, Kallich JD, et al. The Economic Burden of Anemia in Cancer Patients Receiving Chemotherapy. *Value Health*. 2005;8(2):149-156.
  16. Demetri GD, Kris M, Wade J, Degos L, Cella D. Quality-of-life benefit in chemotherapy patients treated with epoetin alfa is independent of disease response or tumor type: results from a prospective community oncology study. *J Clin Oncol*. 1998;16(10):3412-3425.
  17. Glaspy J, Bukowski R, Steinberg D, Taylor C, Tchekmedyan S, Vadham-Raj S. Impact of therapy with epoetin alfa on clinical outcomes in patients with non-myeloid malignancies during cancer chemotherapy in community oncology practice. *J Clin Oncol*. 1997;15(3):1218-1234.
  18. Pirker R. Darbepoetin alfa for the treatment of cancer-related anemia: an update. *Expert Rev Anticancer Ther*. 2004;4(5):735-744.
  19. Herrington JD, Davidson SL, Tomita DK, Green L, Smith RE, Boccia RV. Utilization of darbepoetin alfa and epoetin alfa for chemotherapy-induced anemia. *Am J Health Syst Pharm*. 2005;62(1):54-62.
  20. Schwartzberg LS, Yee LK, Senecal FM, et al. A randomized comparison of every-2-week darbepoetin alfa and weekly epoetin alfa for the treatment of chemotherapy-induced anemia in patients with breast, lung, or gynecologic cancer. *Oncologist*. 2004;9(6):696-707.
  21. Folloder J. Effects of darbepoetin alfa administered every two weeks on hemoglobin and quality of life of patients receiving chemotherapy. *Oncol Nurs Forum*. 2005;32(1):81-91.
  22. Beveridge RA, Rifkin RM, Moleski RJ, et al. Impact of long-acting ESPs on practice dynamics and patient satisfaction. *Pharmacotherapy*. 2003;23(12 pt 2):101S-109S.
  23. Kotasek, D, Steger, G, Faught, W, et al. Darbepoetin alfa administered every 3 weeks alleviates anaemia in patients with solid tumours receiving chemotherapy; results of a double-blind, placebo-controlled, randomized study. *Eur J Cancer*. 2003;39(14):2026-2034.
  24. Canon JL, Vansteenkiste J, Bodoky G, et al. Randomized double-blind active-controlled trial of every-3-week darbepoetin alfa for the treatment of chemotherapy-induced anemia. *J Natl Cancer Inst*. 2006;98(4):273-284.
  25. Taylor K, Ganly P, Charu, V, et al. Randomized double-blind placebo-controlled study of darbepoetin alfa every 3 weeks for the treatment of chemotherapy-induced anemia. *Blood*. 2005;106(11):3556 (abstract).
  26. Rearden TP, Charu V, Saidman B, et al. Results of a randomized study of every three-week fpdomg (Q3W) pf darbepoetin alfa for chemotherapy-induced anemia (CIA). *J Clin Oncol*. 2004;22(14S):8064 (abstract).
  27. Silberstein P, Baccia R, Lie D, et al. Evaluating darbepoetin alfa administered at 300 mcg every three weeks to treat chemotherapy-induced anemia in breast cancer patients. Poster and abstract presented at The 29<sup>th</sup> Annual San Antonio Breast Cancer Symposium, December 10, 2005:5032.
  28. Rodgers GM, Cella D, Chanan-Khan A, et al. Practice Guidelines in Oncology – v.2.2005: Cancer- and Treatment-Related Anemia. The Complete Library of NCCN Clinical Practice Guidelines in Oncology (CD-ROM), April 2005.
  29. Adamson, RA, Baribeault, D, Griffith, N, et al. Contemporary Growth Factor Management: Three Institutional Perspectives. *Hosp Pharm*. (Special Issue - Therapeutics Insights and Review). 2006:1-16.
  30. Hafford A, Griffith N, Seonne-Vazquez E, Szeinbach S. Impact of a pharmacist-directed anemia management program on guideline adherence. Accepted for Professional Poster Presentation, ASHP Midyear Clinical Meeting, Las Vegas, NV; December 2007. ■