NEW ANEMIA GUIDELINES AT OHIO STATE UNIVERSITY: ON-TIME INTERVENTION AND LONGER DOSING INTERVALS ASSOCIATED WITH IMPROVED OUTCOMES IN LYMPHOMA PATIENTS

Based on a poster presented by Nelson M and Buckner M
Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, Ohio

The impact of new guidelines for the treatment of chemotherapy-induced anemia (CIA) was evaluated in a retrospective chart review (n = 81) conducted at the Ohio State University (OSU) Medical Center. The OSU Medical Center’s new supportive care guidelines were developed following review of the literature and the National Comprehensive Cancer Network’s clinical practice guidelines for anemia in patients with lymphoma and stipulated initiating intervention at higher hemoglobin (Hgb) concentrations (<11 g/dL) with darbepoetin alfa every 2 weeks (200 µg) or every 3 weeks (300 µg).1 Darbepoetin alfa was administered subcutaneously and the dose titrated to maintain Hgb levels of 11 to 12 g/dL.

The incorporation of these CIA guidelines may result in improved patient outcomes. Only 6% of patients with a baseline Hgb of at least 10 g/dL required transfusions, emphasizing the effectiveness of early intervention. Patients in the every-3-weeks study arm received synchronized darbepoetin alfa and chemotherapy regimens, minimizing the total number of injections received. However, record review revealed a lack of patient-reported fatigue and iron evaluations. The OSU Medical Center has since included fatigue scores and iron deficiencies in its CIA supportive care guidelines. Oncology nurses were recognized as being well situated to identify borderline Hgb levels and work with clinicians to implement guidelines, thereby improving patient outcomes.

REFERENCE


IS YOUR CHEMOTHERAPY PATIENT IRON DEFICIENT?

Based on a poster presented by Morehead L*; McNulty V†; Zobec A†; and Hicks B†
*Genentech, Colorado Springs, Colorado; †Cancer Center of Colorado Springs, Colorado Springs, Colorado

Despite the benefits of erythropoiesis-stimulating proteins (ESP) for managing chemotherapy-induced anemia (CIA), undetected iron deficiencies can lead to a failure to respond to ESPs in as many as 30% to 50% of patients.1 This failure occurs despite recommendations for a thorough assessment of anemia causes before ESP treatment, including iron assessments, by the

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*This material was developed independently and without review by the Oncology Nursing Society (ONS). ONS does not assume responsibility for the accuracy of this material or opinions expressed herein.

THE ROLE OF THE ONCOLOGY NURSE IN PRECHEMOTHERAPY NEUTROPENIC RISK ASSESSMENT AND PATIENT OUTCOMES

Based on a poster presented by Doyle A; Keegan K; Mullen K; Zecha G; Boyd C; Hutsen J
Puyper Sound Veterans Administration Medical Hospital, Seattle, Washington

Because neutropenia is a common result of myelosuppressive chemotherapy, there is a
need to identify patients at high risk for this complication before therapy to provide growth factor support. Use of a neutropenic risk assessment tool, consistent with recommendations from the National Comprehensive Cancer Network’s clinical practice guidelines, may improve patient outcomes. The nursing staff of Puget Sound Veteran’s Administration Medical Center’s Cancer Care Clinic completed a neutropenic risk assessment for all new patients beginning chemotherapy. Starting with their first cycle of chemotherapy, patients identified as at-risk for neutropenia received granulocyte colony-stimulating factor (G-CSF) support. To evaluate the impact of the tool on patient outcomes, a chart review was performed on patient records before the initiation of the assessment tool (2004) and compared with patient records following the initiation of the assessment tool (2005).

The results demonstrated that the neutropenic risk assessment tool significantly benefited patient outcomes. Compared with data from 2004, the data from 2005 demonstrated a decreased number of hospitalizations for febrile neutropenia (FN; 9.7% vs 2.1%, *P* = .003) and number of hospitalization days (117 days vs 24 days). Proactive use of G-CSF decreased from 10% to 6%. There was a steady increase in the use of G-CSF proactively, as demonstrated by an increase in use from 26% of patients initiating chemotherapy to 51% of patients initiating chemotherapy during the first and last half of 2005, respectively. Moreover, proactive use of G-CSF was strongly associated with myelosuppressive chemotherapy regimens that are known to have high incidence rates (>20%) of FN. Thus, the neutropenic risk assessment, completed by oncology nurses before initiating chemotherapy, was an effective measure to improve patient outcomes.

### PREVENTION OF MUCOSITIS IN AUTO BONE MARROW/STEM CELL TRANSPLANT PATIENTS

**Based on a poster presented by Klocke J*, Cannon M†; Gissinger D†; Bayer R†; Devoe C†; John V†**

*North Shore University Hospital, New York, New York; †North Shore University Hospital, Manhasset, New York*

Approximately 80% of patients who undergo high-dose chemotherapy before bone marrow/autologous stem cell transplantation (SCT) develop mucositis—a painful complication characterized by oral ulceration, epigastric discomfort, diarrhea, rectal irritation (45% vs 85%), shorter hospital stays (28.3 days vs 32.3 days), and a trend toward earlier engraftment. The beneficial effects of palifermin on mucositis symptoms may decrease healthcare costs and improve QOL for patients undergoing SCT.

### SELECTED ABSTRACTS AND POSTER PRESENTATIONS

The following summaries are based on abstracts and posters presented at the 2006 American Society of Clinical Oncologists Annual Meeting held June 2-6, 2006, in Atlanta, Georgia.*†

**DARBEPOETIN ALFA ADMINISTERED AT VARYING INTERVALS COMPARED WITH WEEKLY EPOETIN ALFA FOR TREATING CHEMOTHERAPY-INDUCED ANEMIA: A POOLED ANALYSIS OF 20 CLINICAL TRIALS**

**Based on an abstract presented by Glaspy J; Henry D; Canon J; Lam H; Lillie T**

*University of California Los Angeles Medical Center, Los Angeles, California; Pennsylvania Oncology/Hematology Associates, Philadelphia, Pennsylvania; Centre Hospitalier Notre Dame et Reine Fabiola, Charleroi, Belgium; Amgen Inc., Thousand Oaks, California*

Chemotherapy-induced anemia (CIA) often results in increased risks for blood transfusions and fatigue. Erythropoiesis-stimulating agents (ESA), including epoetin alfa and darbepoetin alfa, have been proven to reduce these risks in patients with CIA. Because darbepoetin alfa has a long half-life (74 hours), it can be dosed weekly, every 2 weeks, or every 3 weeks.† This study evaluated whether these different dosing schedules affected the efficacy of darbepoetin alfa.

Data were pooled from 20 single-arm, active-controlled, and placebo-controlled trials in patients with CIA. Placebo or epoetin alfa was used as the comparator in all controlled trials. Endpoints for the analysis included: the percentage of patients who required transfusions (from week 1 and from week 5 to the end of the treatment period), the percentage of patients who reached a target hemoglobin (Hgb) level of at least 11 g/dL, and the percentage of patients who experienced at least a 3-point change in the Functional Assessment of Cancer Therapy: Fatigue score from...
baseline. Percentages were adjusted for baseline Hgb levels (<10 g/dL vs ≥10 g/dL), type of chemotherapy regimen (platinum vs non-platinum), and dosage adjustments. Logistic regression with treatment as a random effect was used to analyze the results.

Clinically meaningful endpoints were reached equally across types and dosing schedules of ESA treatment analyzed (Table). The efficacy of darbepoetin alfa, administered every week, every 2 weeks, or every 3 weeks, was comparable to epoetin alfa every week. These data support the synchronous use of darbepoetin alfa flexible dosing with chemotherapy regimens, which may reduce the number of clinic visits for patients.

FINAL RESULTS OF A RANDOMIZED STUDY COMPARING 2 DOsing REGIMENS OF EPOETIN ALFA IN PATIENTS WITH CHEMOTHERAPY-INDUCED ANEMIA: 80 000 U EVERY 2 WEEKS VERSUS 40 000 U WEEKLY

Based on an abstract presented by Henry DH; Kamin M; Wilhelm F; Williams D; Xie J; Woodman RC
Joan Karnell Cancer Center, Philadelphia, Pennsylvania; Ortho Biotech Clinical Affairs, LLC, Bridgewater, New Jersey; Johnson & Johnson Pharmaceutical Research and Development, LLC, Raritan, New Jersey

The standard once-weekly administration of epoetin alfa is inconvenient for patients because of the frequency of clinic visits. This randomized, open-label, 13-week study of patients with nonmyeloid malignancies evaluated extended interval initial dosing with epoetin alfa 80 000 U every 2 weeks compared to the standard 40 000 U weekly regimen. Patients entering the study had baseline hemoglobin (Hgb) levels of 11 g/dL or less and chemotherapy planned for at least 12 weeks.

Epoetin alfa treatment was temporarily discontinued when Hgb levels reached more than 13 g/dL, and dose reductions were instituted when Hgb was greater than 12 g/dL or rose by more than 1 g/dL in any 2-week period. Patients in the 80 000 U every-2-weeks arm with inadequate Hgb responses were switched to a dose of 40 000 U weekly, whereas patients in the 40 000 U weekly arm with inadequate Hgb responses were increased to a dose of 60 000 U weekly. The primary outcome was mean change from baseline to end-of-study in Hgb levels.

Baseline characteristics were comparable between the epoetin alfa weekly (n = 145) and epoetin alfa every-2-weeks (n = 153) groups. The mean baseline Hgb was 10 g/dL and common cancer types were breast (25%), non-small cell lung

Table. Patients Achieving Clinically Meaningful Endpoints with ESA Treatment

<table>
<thead>
<tr>
<th>DA Every 3 Weeks (n = 5 studies)</th>
<th>DA Every 2 Weeks (n = 7 studies)</th>
<th>DA Every Week (n = 6 studies)</th>
<th>EA</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) DA weekly dose</td>
<td>113 (37) µ/wk</td>
<td>119 (303) µ/wk</td>
<td>164 (69) µ/wk</td>
<td>40 340 (21 461) U/wk</td>
</tr>
<tr>
<td>Percent (95% CL) patients with transfusions (wk 5 to EOTP)</td>
<td>28% (24, 31)</td>
<td>27% (23, 30)</td>
<td>33% (29, 38)</td>
<td>27% (23, 31)</td>
</tr>
<tr>
<td>Percent (95% CL) patients achieving target Hgb of ≥11 g/dL</td>
<td>72% (69, 75)</td>
<td>74% (71, 77)</td>
<td>69% (65, 73)</td>
<td>74% (70, 77)</td>
</tr>
<tr>
<td>Percent (95% CL) patients with ≥3-point change in FACT-F score from baseline</td>
<td>45% (42, 48)</td>
<td>51% (48, 54)</td>
<td>43% (39, 46)</td>
<td>40% (36, 43)</td>
</tr>
</tbody>
</table>

*Two patients randomized to receive placebo were administered DA.

CL = confidence limit; DA = darbepoetin alfa; EA = epoetin alfa; EOTP = end of treatment period; ESA = erythropoiesis-stimulating agent; FACT-F = Functional Assessment of Cancer Therapy: Fatigue; Hgb = hemoglobin.

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(15%), and colorectal (14%). Efficacy analysis was performed on 295 patients with at least 1 post-baseline Hgb value \((n = 144\) weekly; \(n = 151\) every 2 weeks). Mean changes in Hgb from baseline to end-of-study were nearly identical between treatment groups (every 2 weeks arm, \(1.27 \pm 1.48\) g/dL; weekly arm, \(1.28 \pm 1.60\) g/dL [difference = 0, 1-sided 95% confidence interval -0.25, -]).

Additional analyses revealed that the post-28 day transfusion rate was 11.2% in the every-2-weeks arm and 12% in the weekly arm (Kaplan-Meier estimates). Dose changes included holds in 21% of the every-2-weeks arm versus 42% of the weekly arm and reductions in 41% of the every-2-weeks arm versus 59% of the weekly arm. Dose switching was required in 13% of the patients receiving epoetin alfa every 2 weeks, whereas 37% of patients receiving epoetin alfa weekly required a higher dose (60,000 U). Clinically relevant thrombotic vascular events and deaths occurred in 7.8% and 6.5%, respectively, of patients in the every-2-weeks group and 7.6% and 6.2% of patients in the weekly group.

This study demonstrated that both dosing regimens of epoetin alfa were similarly effective and tolerated, thus providing a degree of dosing flexibility with epoetin alfa and improved convenience for patients with chemotherapy-induced anemia.

**FINAL RESULTS OF A LARGE, COMMUNITY-BASED, PROSPECTIVE STUDY EVALUATING THE IMPACT OF FIRST AND SUBSEQUENT CYCLE PEGFILGRASTIM ON NEUTROGENIC EVENTS IN PATIENTS RECEIVING MYELOSUPPRESSIVE CHEMOTHERAPY**

Based on an abstract presented by Ozer H; Mirtsching B; Rader M; Ding B; Trusinski D; Dreiling L. University of Oklahoma Cancer Institute, Oklahoma City, Oklahoma; Center for Oncology Research and Treatment, PA, Dallas, Texas; Union State Bank Cancer Center, Nyack, New York; Amgen, Inc., Thousand Oaks, California

In the community practice setting, 8% of patients undergoing chemotherapy with or without growth factor support, had cycle 1 febrile neutropenia (FN), which limits the effectiveness of chemotherapy. This multicenter, open-label study assessed the impact of pegfilgrastim used during first and subsequent cycles of chemotherapy on neutropenic events in patients receiving chemotherapy in the community. Eligible subjects included patients aged 18 or older who had cancers other than leukemia or myelodysplastic syndrome and who where undergoing a minimum of 4 chemotherapy cycles (maximum of 8 cycles). Patients receiving weekly chemotherapy or concurrent radiotherapy were excluded. Pegfilgrastim 6 mg was administered approximately 24 hours after each chemotherapy session. Outcomes included hospitalizations for neutropenia (neutropenia related or FN related), chemotherapy dose reductions and delays, and presence of FN (defined as an absolute neutrophil count \(<1 \times 10^9$/L\) and elevated temperature \(>38.2^\circ C\)).

Results from 2112 patients who received chemotherapy and pegfilgrastim were included in the final analyses. Of the study population, a majority of patients were female (75%) and 36% were aged 65 or older. Fifty-five percent of patients had stage 3/4 or extensive disease, 23% received prior chemotherapy treatment, 17% received prior radiotherapy treatment, and 27% had significant comorbidity. Prevalent cancer types were: breast (46%), lymphoma (18%), lung (16%), and ovarian (8%). Hospitalizations and dose reductions and delays resulting from neutropenia were infrequent (Table). FN was experienced by 3.6% of patients in the first cycle of chemotherapy (95% confidence interval [CI], 2.8, 4.5) and 6.3% of patients in all cycles (95% CI, 5.3, 7.5). Serious adverse events were consistent with chemotherapy-associated toxicities.

These data demonstrated that parallel administration of pegfilgrastim with cycles of myelosuppressive chemotherapy lowered the incidence of neutropenic complications and the need for chemotherapy dose delays and reductions.

**Table. Prevalence of Neutropenic Complications**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Cycle 1% (95% CL)</th>
<th>All Cycles % (95% CL)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For neutropenia</td>
<td>2.9 (2.3, 3.7)</td>
<td>5.6 (4.7, 6.7)</td>
</tr>
<tr>
<td>For febrile neutropenia</td>
<td>1.7 (1.2, 2.3)</td>
<td>3.5 (2.7, 4.3)</td>
</tr>
<tr>
<td>Physician-reported dose reduction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All reasons</td>
<td>7.3 (6.2, 8.5)†</td>
<td>16.8 (15.2, 18.5)</td>
</tr>
<tr>
<td>Reasons due to neutropenia</td>
<td>1.8 (1.2, 2.4)†</td>
<td>2.9 (2.2, 3.7)</td>
</tr>
<tr>
<td>Physician-reported dose delay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All reasons</td>
<td>7.5 (6.4, 8.8)†</td>
<td>20.1 (18.4, 21.8)</td>
</tr>
<tr>
<td>Reasons due to neutropenia</td>
<td>0.9 (0.5, 1.4)†</td>
<td>2.1 (1.5, 2.8)</td>
</tr>
</tbody>
</table>

*Maximum of 8 cycles; †in cycle 2. CL = confidence limit.

A RANDOMIZED PROSPECTIVE OPEN-LABLED STUDY OF ORAL AMOXICILLIN-CLAVULANATE WITH INTRAVENOUS CEFTRIAXONE AND AMIKACIN IN LOW-RISK FEBRILE NEUTROPE尼亚

Based on an abstract presented by Dominic JF; Kumar L; Kochupillai V; Raina V; Sharma A; Bakshi S; Seth T; Kapil A. India Institute of Medical Sciences, New Delhi, India

Low-risk febrile neutropenia (FN) can be treated with empiric oral antibiotics. This randomized, prospective,
open-label trial evaluated patients aged 15 through 75 years with low-risk FN (defined as expected neutropenic duration <7 days with no comorbid features). Patients were randomized to receive oral amoxicillin-clavulanate 625 mg twice daily and levofloxacin 500 mg once daily or intravenous (IV) ceftriaxone 2 g and amikacin 15 mg/kg once daily. The primary endpoint was response to therapy, which was defined as abatement of fever within 72 hours accompanied by improved clinical manifestation of infection and no recurrence of fever for 48 hours in the absence of antipyretics. In the event of treatment failure, growth factor use was permitted.

Sixty-four episodes of FN were evaluated in 53 patients (n = 33 in the IV arm, n = 31 in the oral antibiotics arm). Of these episodes, the accompanying diagnosis was bone and soft tissue sarcomas (n = 32), hematologic cancer (n = 22), and other solid cancers (n = 10). Treatment groups were matched for demographics including age, gender, and type of cancer. Median baseline absolute neutrophil count was 200/µL in both arms; duration of neutropenia was 5 days in the IV arm and 4 days in the oral antibiotics arm. Fifteen percent of FN episodes were clinically identified, whereas 11% were microbiologically identified. Of the microbiologically identified cases, 57% were caused by gram-positive organisms. Response to therapy occurred in 72% (95% confidence interval [CI], 58%–88%) of patients in the IV arm and 77% (95% CI, 63%–92%) of patients in the oral antibiotics arm. Serious toxicity was limited to 1 patient in the IV group who experienced convulsions. No mortality was reported in either group. Second-line IV antibiotics were given to all patients failing treatment. Equivalence, using a 25% difference between treatment arms as unequal, was demonstrated with a power of 59% (P = .03). These data demonstrated that oral and IV antibiotics have comparable efficacy in managing low-risk FN.

**ORAL MUCOSITIS-RELATED MORBIDITY AND RESOURCE UTILIZATION IN A PROSPECTIVE STUDY OF HEAD AND NECK CANCER PATIENTS**

Based on an abstract presented by Isitt J; Murphy BA; Beaumont JL; Garden AS; Gwede CK; Trotti A; Meredith RF; Epstein JB; Le Q; Brizel DM; Oral Mucositis Study Group. Amgen Inc., Thousand Oaks, California; Vanderbilt University, Nashville, Tennessee; Northwestern University, Evanston, Illinois; University of Texas MD Anderson Cancer Center, Houston, Texas; Moffitt Cancer Center, Tampa, Florida; University of Alabama, Birmingham, Alabama; University of Illinois, Chicago, Illinois; Stanford University, Stanford, California; Duke University, Durham, North Carolina.

The effects of complications of oropharyngeal mucositis (OM) following head and neck cancer (HNC) treatment, in addition to the resulting resource consumption, are not well studied. This 6-week, multicenter, prospective, single-arm, observational study evaluated outcomes in patients receiving radiation, with or without chemotherapy, for HNC.

Patients completed the Oral Mucositis Weekly Questionnaire-Head and Neck, which assesses severity and impact of OM, 5 times during the study, and their resource use was collected on a biweekly basis. Hospitalization costs were determined based on the Healthcare Utilization Project Nationwide Inpatient Sample (HUPNIS).

Results indicated a high prevalence of opioid use (85% [95% CI, 75%–92%]), severe mouth and throat soreness (76% [95% CI, 65%–85%]), and concurrent chemoradiation (67% [95% CI, 55%–77%]). Seventy-eight percent (95% CI, 68%–86%) of opioid use was attributable to mouth and throat pain. Severe difficulty swallowing was reported by 38% (95% CI, 26%–50%) of patients during study weeks 1 and 2, of whom 67% took opioids. By week 6, severe difficulty swallowing was reported by 59% of patients, of whom 84% received opioids. Fifty-one percent (95% CI, 39%–62%) of patients required a feeding tube. Hospitalizations were reported for 37% of patients (95% CI, 26%–49%), but only 30% (95% CI, 16%–49%) were related to mucositis. Patients spent a mean of 4.9 days in the hospital (range, 1–16 days; SE, 0.72), which equated to a national average cost of approximately $23 000 (SE, $565) based on HUPNIS data for a 5-day hospital stay. This study demonstrated that patients treated for HNC incur a high prevalence of OM and that its associated burden to patients and healthcare costs may benefit from effective strategies to alleviate OM.