Relative Dose Intensity: Improving Cancer Treatment and Outcomes

Cheryl Lenhart, BSN, HRM

This article has been chosen as being particularly suitable for reading and discussion in a Journal Club format. The following questions are posed to stimulate thoughtful critique and exchange of opinions, possibly leading to changes on your unit. Formulate your answers as you read the article.

1. Is this article research based? What level of evidence is presented?
2. What rate of dose delays or changes do our patients experience? Has this rate been determined systematically?
3. What are the common reasons among our patient population for dose delays or reductions?
4. How formal is our process for determining dose delays or reductions? Is the process protocol based? Is a written order required?
5. When providing patient education regarding chemotherapy, do we regularly discuss the importance of maintaining doses and schedules as strictly as possible with the patient and family?
6. What specific strategies can we implement to increase compliance with ideal dose and schedule requirements?

At the end of the session, take time to recap the discussion and make plans to follow through with suggested strategies.

Purpose/Objectives: To determine the incidence of and reasons for chemotherapy dose delays or reductions.

Design: A performance improvement initiative formed the basis for a prospective nursing research study.

Setting: A single institution in western Pennsylvania.

Sample: 204 patients scheduled for nonmyeloablative chemotherapy.

Methods: Data collection forms were completed by RNs and evaluated by an interdisciplinary team.

Main Research Variables: Rates of nonadherence to chemotherapy schedule or dosing and associated reasons.

Findings: The performance improvement initiative revealed evidence of nonadherence to chemotherapy schedule or dosing when patient-requested cancellations and physician-ordered dose delays and reductions were left unchallenged and medical and nursing staffs had limited knowledge of or interest in relative dose intensity. The ensuing nursing research study found that less than 51% and 78% of patients adhered to their schedule and dosage, respectively. Nonadherence primarily was attributed to canceled visits, suboptimal or nonuse of hematopoietic growth factors, and routine dose reductions. Subsequent educational initiatives targeting the interdisciplinary team and patients and their families focused on the importance of keeping scheduled visits and preventing versus managing pancytopenia. Adopting a telephone referral procedure and distributing a patient education sheet reduced patient cancellations by 50%. Various reasons for dose delays and reductions have surfaced, many of which are modifiable with educational efforts.

Conclusions: A knowledge deficit was found among patients and healthcare providers regarding the importance of adhering to chemotherapy orders.

Implications for Nursing: Evaluating patterns of chemotherapy administration and educating patients, nurses, and physicians will have an impact on relative dose intensity, potentially improving treatment outcomes.

Key Points . . .

- Maintaining the relative dose intensity of chemotherapy is key to increasing overall survival and achieving long-term disease-free survival.
- The relative dose intensity is the percentage of the planned chemotherapeutic dose a patient receives over a given time period.
- Relative dose intensity is affected by patient visit cancellations, dose reductions, under- or nonuse of hematopoietic growth factors, and deviation from original chemotherapy orders.
- Educating interdisciplinary staff about the importance of relative dose intensity and educating patients about the need for adherence to scheduled treatment visits can increase relative dose intensity and minimize dose delays and reductions.

Cheryl Lenhart, BSN, HRM, is a nurse manager in the Bone Marrow Transplant Unit and the Medical Short Stay Center at the Western Pennsylvania Hospital in Pittsburgh. She is a member of the visiting speaking bureau for Wyeth Pharmaceuticals Inc., manufacturer of Neumega®, and the speakers bureau for Amgen Inc., manufacturer of Aranesp®, Neupogen®, and Neulasta®, which are mentioned in this article. *Partial funding for development of this article was provided by Wyeth Pharmaceuticals Inc. (Submitted May 2004. Accepted for publication October 5, 2004.)* *(Mention of specific products and opinions related to those products do not indicate or imply endorsement by the* Oncology Nursing Forum *or the Oncology Nursing Society.)*

Digital Object Identifier: 10.1188/05.ONF.757-764

As the treatment of patients with cancer continues to evolve with the development of more effective chemotherapeutic drugs and combination regimens, emphasis has increased regarding maintaining dose intensity and preventing dose delays in clinical practice. These two factors have been known to critically influence patient outcomes. Studies have shown that delayed or dose-reduced chemotherapy cycles that result in a lower dosage per unit time or relative dose intensity (RDI) diminish the killing of tumor cells (Frei & Canellos, 1980) and can have a great impact on long-term disease-free and overall survival (Bonadonna, Valagussa, Moliterni, Zambetti, & Brambilla, 1995; Budman et al., 1998; Epelbaum, Haim, Ben-Shahar, Ron, & Cohen, 1988; Kwak, Halpern, Olshen, & Horning, 1990).

An early retrospective study of 115 patients with large-cell lymphoma treated with cyclophosphamide, doxorubicin, and vincristine-based chemotherapy found that an actual doxorubicin RDI of 75% or greater was the most important predictor of survival (Kwak et al., 1990). The average RDI of all agents comprising four- or six-drug regimens also was a significant prognosticator for survival on multivariate analysis. Subsequently, Bonadonna et al. (1995) reported the 20-year outcomes of adjuvant cyclophosphamide, methotrexate, and 5-fluorouracil for 386 patients who underwent radical mastectomy for node-positive breast cancer. When patients received at least 85% of the planned chemotherapy dose, relapse-free and overall survival rates were 49% and 52%, respectively; in the subset treated with less than 65% of the planned dose, the corresponding rates of 30% and 25%, respectively, were virtually identical to those reported for chemotherapy-naive women.

Dose reduction is a commonly used strategy for ameliorating chemotherapy-induced toxicity. Clinical data convincingly support the premise of RDI and its direct impact on long-term outcomes, yet most clinicians try to minimize myelosuppression by reducing the dose of chemotherapy or prolonging chemotherapy intervals. In clinical research and practice settings, myelotoxicity is the most prominent reason for delaying or dose-reducing chemotherapy (Epelbaum et al., 1988; Frasci, 2002; Kwak et al., 1990; Pettengell et al., 1992). The availability of hematopoietic growth factors such as granulocyte colony-stimulating factor, with its ability to maintain the dose intensity of myelotoxic chemotherapy regimens (Pettengell et al.), has raised the potential for improving disease-free and overall survival through supportive care.

Many cancer centers and individual units and departments have improved the delivery of chemotherapy to their patients by expediting the pharmacy preparation of chemotherapy, improving chemotherapy delivery methods, and standardizing physician ordering pathways. However, few have formally studied their chemotherapy practices to determine the reasons for and consequences of deviating from original chemotherapy orders.

At the Western Pennsylvania Hospital in Pittsburgh, performance improvement initiatives require the identification of a targeted improvement for each nursing unit or department. Meetings with the oncology Performance Improvement Team resulted in substantial discussion regarding the evaluation of chemotherapy administration practices, and approval was given to proceed with determining whether patients were adhering to their chemotherapy schedule and dosing amount. Although the staff agreed to proceed with this challenging targeted improvement, most staff members were convinced that a majority of patients were receiving their chemotherapy as originally ordered.

Performance Improvement Initiative

Data Collection

Clinical information was obtained using a data collection sheet to capture patients' admission data, laboratory data on scheduled chemotherapy days, dates and cycles of scheduled chemotherapy, reasons for any dose reductions or delays, and use of hematopoietic growth factors. No patient consent was obtained because only data were collected; therefore, no active patient involvement was necessary.

In an effort to develop practice recommendations for a formal nursing research proposal, all data sheets collected during a six-month period were reviewed in detail, and members of the nursing staff were interviewed to further elucidate existing clinical practice patterns.

Key Findings

Nonadherence to chemotherapy schedule or dosing was readily apparent, as evidenced by an acceptance of physician orders for chemotherapy visit cancellations and dose reductions, an acceptance of patient self-cancellations, and a lack of understanding of key concepts related to tumor-cell death and the overall effectiveness of chemotherapy. More specifically, dose reductions were permitted without specification of the criteria, chemotherapy orders were being used that had standardized instructions for holding and dose-reducing chemotherapy (rather than an individualized approach), and patients were able to cancel their scheduled visit without speaking to a physician or nurse.

Several modifiable challenges associated with the data collection, including an unclear chemotherapy schedule on the initial physician order, failure to attach the original chemotherapy order to the data collection sheet, use of scheduled rather than actual days of treatment on the data sheet (making determining whether a patient actually missed treatment difficult), incomplete forms, and a lack of explanation for dose reductions, were identified early on. Four main barriers to optimal chemotherapy administration practices also surfaced on review of the early data: (a) patient visit cancellations, (b) dose reductions, (c) under- or nonuse of hematopoietic growth factors, and (d) deviation from the original chemotherapy orders in the majority of patients.

Misunderstanding of the targeted improvement was apparent in that most RN caregivers had no working knowledge of the concept of RDI and limited understanding of its role in each patient's final outcome. Other members of the interdisciplinary team, including the physicians, generally had some working knowledge of RDI but did not appear to be highly interested in this concept. Therefore, the nursing and interdisciplinary staff were required to attend in-service workshops to enhance their understanding of the concept of RDI (see Figure 1) and their roles in this ongoing initiative.

Nursing Research Study of Relative Dose Intensity

As discouraging as the preliminary performance improvement results and understanding of the RDI-related concepts

- Definition of relative dose intensity, dose escalation, and dose intensification
- Optimizing chemotherapy regimens for maximum cell death
- Tumor cell growth
- Expected treatment outcomes
- Common causes of dose modifications to planned chemotherapy regimens

Figure 1. Important Concepts Related to Relative Dose Intensity

were, the Performance Improvement Team believed that studying chemotherapy administration practices was extremely important. Retrospectively, however, the significance of these data still was underestimated. Given that the Performance Improvement Team appeared to be on the brink of uncovering substantial information and had a strong desire to relate it to nursing and medical practices, a nursing research proposal (also aimed at soliciting interest and appreciation among nursing caregivers) was submitted. The purpose of the ensuing study was to identify the incidence of patients who do not receive their scheduled course of chemotherapy, as well as to explain its occurrence, and to suggest recommendations for practice to support cancer treatment goals. The first steps were to address patient cancellations and reasons for the cancellations (calling on the nursing staff, physicians, certified nurse practitioners, and secretarial staff), encourage patients to reschedule for the next day rather than for the same day the following week, educate the interdisciplinary team on RDI, and improve the tracking of laboratory values on the data collection sheet.

Data Collection and Analysis Procedures

The target sample size was 250 patients scheduled for all types of nonmyeloablative chemotherapy at the Western Pennsylvania Hospital. The data collection process was not associated with any limitations or potential hazards to participating subjects.

Data collection began on August 1, 2002, and is scheduled to continue until 250 patients are studied; 204 patients had been evaluated as of September 2003. The RN caregiver was responsible for completing the data collection form for every scheduled day and dose of chemotherapy. The form was kept with patients' charts and collected when patients were discharged.

The data were analyzed on a monthly basis by the coinvestigators. All data fields were completed and grouped according to 11 categories: diagnosis, type of cancer and stage, regimen or protocol, number of scheduled cycles successfully completed, number of scheduled cycles delayed, number of scheduled cycles the dose was reduced, planned dose of chemotherapy, actual dose of chemotherapy received, RDI received, reasons for delay or reduction, and person canceling the visit or admission. Recommendations for clinical practice were made by the coinvestigators in conjunction with the nursing manager.

Because July 2002 marked the beginning of the 2003 fiscal year and data collection began on August 1, 2002, complete data were only available for the second, third, and fourth quarters.

Key Findings

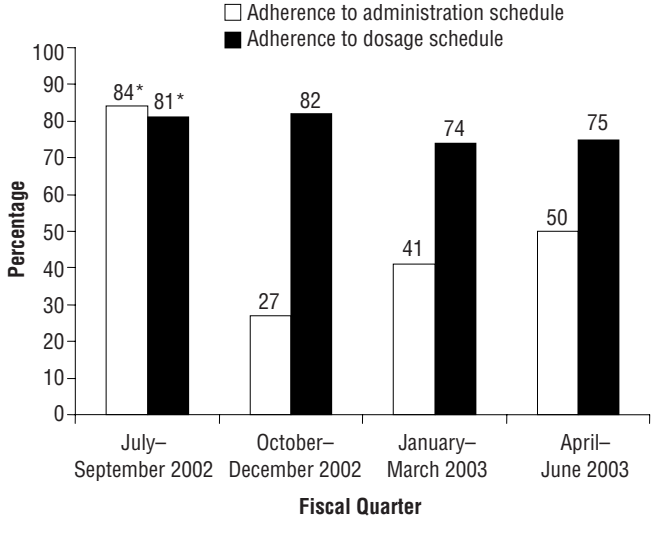
The proportions of patients adhering to their chemotherapy schedule and dosage were less than 51% and 78%, respectively, falling below the prespecified yearly goal of more than 90%. During the second, third, and fourth quarters, adherence to the schedule was substantially lower than adherence to the dosage (see Figure 2).

Second quarter: From October–December 2002, 35 patients were followed and all cancellations, changes in the visit date, and dose reductions were recorded. The results of the second quarter data collection illustrated that strict adherence to the proposed chemotherapy regimen was not occurring for a variety of reasons. The three main reasons for nonadherence were (a) canceled visits from various sources (patient, family, physician office); (b) ill-timed use, underuse, or nonuse of hematopoietic growth factors; and (c) routine dose reductions of chemotherapy with no apparent explanation. The Performance Improvement Team continued to collect and analyze the data and implemented recommendations for gathering additional types of data (i.e., cycles, dates, blood counts, use of growth factors, platelet transfusions, delays, dose reductions, changes in medications, reasons for changes, and visit cancellations noting the reason and person canceling).

The most challenging aspect of the performance improvement recommendations was teaching RDI in a way that RN caregivers could understand and self-calculate (see Figure 3). This was deemed paramount to eliciting the degree of nurse participation that was critical to the accuracy of the data collection and to ensuring the advocacy role of the RN caregiver in gaining patient schedule and dose compliance. Additional topics of the nursing education included tumor cell response to chemotherapy, the Gompertzian model of cyclical dosing (Norton, 1988), a review of adjuvant chemotherapy goals, and a discussion of myelosuppression with a focus on pancytopenia (i.e., anemia, neutropenia, and thrombocytopenia).

Two examples of RDI calculations in actual patients follow.

Case study 1: A 67-year-old man with prostate cancer was scheduled for eight weeks of chemotherapy with leucovorin



* Data are from September only.

Figure 2. Adherence to Chemotherapy Schedule and Dosage by Fiscal Quarter

Equations

Planned dose intensity (PDI) = planned total chemotherapy dose (mg or mg/m^2)/planned time to complete chemotherapy (weeks)

Delivered dose intensity (DDI) = total actual delivered dose (mg or mg/m^2)/actual time to complete chemotherapy (weeks)

Relative dose intensity (RDI) = (delivered dose intensity/planned dose intensity) × 100%

Examples

- Initial physician order: chemotherapy 100 mg per week every three weeks for six cycles (total of 18 weeks)
  - If all cycles were administered as ordered
    Total dose = 1,800 mg (100 mg × 18 weeks)
    PDI = 100 mg per week (1,800 mg/18 weeks)
    DDI = 100 mg per week (1,800 mg/18 weeks)
    RDI = 100% ([100 mg per week/100 mg per week] × 100%)
  - If all cycles were delayed by one week
    Total dose = 1,800 mg
    Total length of therapy = 24 weeks (6 cycles × 4 weeks)
    DDI = 75 mg per week (1,800 mg/24 weeks)
    RDI = 75% ([75 mg per week/100 mg per week] × 100%)[a]
  - If all cycles were delayed by one week and the last two cycles were dose reduced by 25%
    Total dose = 1,650 mg ([100 mg × 12 weeks] + [100 mg × 0.75 × 6 weeks])
    Total length of therapy = 24 weeks
    DDI = 69 mg per week (1,650 mg/24 weeks)
    RDI = 69% ([69 mg per week/100 mg per week] × 100%)[b]

[a] The patient received 75% of the chemotherapy in the dose or time frame originally ordered by the physician.

[b] The patient received 69% of the chemotherapy in the dose or time frame originally ordered by the physician.

Figure 3. Calculating Relative Dose Intensity

500 mg/m^2 weekly, cyclophosphamide 500 mg/m^2 weekly, and pamidronate 90 mg over two hours every month. A complete blood count was obtained weekly before chemotherapy, which was to be held for an absolute neutrophil count less than 1,500/mcl or for a platelet count less than 90,000/mcl. The patient's treatment goal was to be cured. Per the original chemotherapy orders, 8,000 mg of cyclophosphamide was to be administered over a total of eight weeks, at a planned dose intensity of 1,000 mg per week. The treatment course, however, was delayed for four weeks: one week for fever of unknown origin, one week for severe dehydration, and two weeks for a platelet count less than 70,000/mcl. Given that the actual time to complete the regimen was 12 weeks, the delivered dose intensity was 667 mg per week (8,000 mg divided by 12 weeks) and the RDI was 67% ([667 mg per week divided by 1,000 mg per week] multiplied by 100%). Eliminating only the platelet-related delays would have resulted in a substantially higher RDI of 80%.

Case study 2: A 47-year-old man admitted with a diagnosis of non-Hodgkin lymphoma was scheduled to receive four cycles of CHOP chemotherapy (cyclophosphamide 3.5 g, vincristine 2 mg, doxorubicin 83 mg [50 mg/m^2 multiplied by 1.65], and oral prednisone 100 mg). The original chemotherapy orders specified dose modification if the absolute neutrophil or platelet counts reached thresholds of less than 1,500/mcl or less than 90,000/mcl, respectively. The actual treatment course was prolonged by two one-week delays—once for fever and once for low platelets—and the last dose was reduced by 20%. Planned and delivered dose intensities for doxorubicin were 83 mg per week (332 mg divided by four weeks) and 52.5 mg per week (315 mg divided by six weeks), respectively, for an RDI of 63% (52.5 mg per week divided by 83 mg per week). The three other agents comprising the CHOP regimen were affected to the same degree. Again, to understand just how significant every dose reduction and delay is to the final RDI, if just one of the platelet delays could have been eliminated, the final RDI for this patient would have been 76%—a substantial improvement over his actual RDI.

Third quarter: By the third quarter of the fiscal year (January–March 2003), trends emerged that were alarming yet invaluable in revealing opportunities for notable improvements. In this regard, the primary focus was twofold: (a) Assess patients to determine the appropriateness of growth factors for preventing versus managing anemia, neutropenia, and thrombocytopenia, and (b) educate patients and families about keeping visits and maintaining health, thereby increasing the chances of receiving maximum chemotherapy. Beginning July 1, 2003, all patient or family calls to cancel a chemotherapy visit were required to be referred to a nurse. Patient information sheets for new chemotherapy recipients were developed that stressed the importance of adhering to the scheduled course of chemotherapy (see Figure 4). These information sheets represented the first time that patients received materials addressing the rationale for adhering to their scheduled chemotherapy regimen. Since distributing this teaching tool and initiating the telephone referral procedure, the number of patient cancellations has been reduced by 50%—from an average of 10–12 per week at the beginning of the study to 5–6 per week by the end of the fourth quarter. As an additional measure, in May 2003, the Performance Improvement Team recommended to the oncology panel (i.e., adminstration personnel responsible for overseeing oncology operations) that physicians be responsible for documenting the specific reason for dose reduction.

Fourth quarter: From April–June 2003, a total of 68 chemotherapy recipients were studied. In this quarter, a variety of reasons were found for dose delays and reduction (see Figure 5). For example, physician orders contained parameters to hold or reduce chemotherapy based on predetermined laboratory values, and dose reductions and delays occurred without documented rationale and were essentially unchallenged by RN caregivers.

Reasons for Patient Visit Delays

Delays in receiving ordered doses of chemotherapy fell into three categories: visit cancellations, knowledge deficit, and noncompliance despite recognizing the significance of keeping scheduled visits. The most frequent causes of patient self-cancellations were "feeling ill" and the desire to attend social functions. Myelosuppression and fever were the most frequent medical causes for cancellation. A combination of visit cancellations and change of scheduled day accounted for 26% of the delays; 10% of these changes were made within one day of the intended visit, and 24%

Today _____ you are making your first visit for chemotherapy in the Medical Short Stay Center at the Western Pennsylvania Hospital. Please read the following information about what to expect from this treatment.

"Chemotherapy and You"
Please read over the booklet "Chemotherapy and You" that you received from your nurse. This booklet contains information about what to expect during chemotherapy and you can do to take care of yourself before and after treatment.

This booklet is designed to help you become an informed partner in your care. If you have any questions about the content, ask your nurse or doctor for further explanation. Do not be afraid to ask questions.

Understanding Your Medicines
The nurse will review with you the names of your chemotherapy medicines, other medications the doctor has ordered for you, how these drugs work, and what side effects you can expect. If you would like to know more about the medicines you will be receiving, ask your nurse. We can provide you with information sheets about most medications.

Keeping Your Appointments
It is very important for you to keep your appointments for treatments. Your nurse will review with you the dates you are scheduled for treatments. If you have any problem keeping your appointments, let your nurse know so that we can try and help prevent any delays.

Our goal is to make sure that you receive your chemotherapy as the doctor ordered. This means that you need to take care of yourself during treatment, get your blood drawn for testing, and come to your chemotherapy appointments **on the days you are scheduled.**

If you feel you cannot make your appointment:
- You must call your doctor. Your doctor will want to talk with you and may need to see you.
  Your doctor's name _____ Phone number: _____
- You also must call the Medical Short Stay Center at (provide phone number) and ask to talk to a nurse.

Local Support Groups
There are local support groups that can get you in touch with people who are having similar treatments. Talking with people who understand what you are going through can be a very good way of helping yourself during this time. Here are telephone numbers for some Pittsburgh-area support groups:
- The American Cancer Society: (provide phone number)
- Cancer Caring Center: (provide phone number)
- United Way of Allegheny County: (provide phone number)
- Magee Women's Selp-Help Groups: (provide phone number)

Communicate With Others
Be open and honest with others about how your treatment is going and how you feel about it. In that way, misunderstandings can be avoided and others are given the chance to support you. Write down **any questions or concerns** you have so that you can remember to ask your doctor or nurse about them.

Side Effects of Chemotherapy
The nurse will review with you some of the symptoms you may have with chemotherapy. It is important to remember that you are receiving some powerful medicines to fight your cancer. They may also cause some side effects. If you have any of these symptoms (side effects), or if you experience anything that is unexpected or that concerns you, make sure that you tell your doctor or your nurse. Knowing about these symptoms as early as possible helps us fight back with supportive medications that can make you feel better.

Finally . . .
Finally, remember that from treatment cycle to treatment cycle, you will have good days and bad days. No two patients respond exactly the same way to chemotherapy. It may be helpful to know that **others care about you.** The staff of the Medical Short Stay Center will do our best to help you in any way we can during your visits.

Figure 4. Information Sheet for Patients on Their First Chemotherapy Appointment

Note. Reprinted with permission from the Western Pennsylvania Hospital.

of the delays were because of low blood counts, fevers, or other illnesses.

Reasons for Chemotherapy Dose Reductions

Identifiable reasons for dose reductions were myelosuppression, under- or nonuse of hematopoietic growth factors, a patient's poor physical condition, and a patient's negative experiences during previous cycles. No reason was apparent for dose reduction in some patients who had blood counts in the normal range and no weight loss or other objective signs of chemotherapy-related toxicity. The action plan included continued monitoring by the Performance Improvement Team and sharing of data obtained from chart reviews with the attending physicians during the first quarter of the 2004 fiscal year.

Discussion

The nursing research found a knowledge deficit among patients and healthcare providers regarding the implications of keeping on schedule with chemotherapy treatments, warranting educational intervention. All patients now receive an instructional sheet at their first chemotherapy appointment, and in addition to a series of staff in-service programs,

Reasons for dose delays

- Visit cancellations
  - Patients: fear, transportation, important dates, caring for spouse or others
  - Family: fear, empathy, important dates
  - Physician: patient illness (e.g., fever, dehydration), patient's low platelet or white blood cell counts, "excusing" patients from visits
- Interdisciplinary team's knowledge deficit
  - Not aware of the importance of keeping visit dates
  - Not aware of relative dose intensity (RDI) concept
- Patients' noncompliance
  - Knows the importance of keeping scheduled visits, but other factors impede the chemotherapy course (e.g., fear, caring for significant other, transportation issues)

Reasons for dose reductions

- Myelosuppression
  - Platelets
  - White blood cells
- Under- or nonuse of hematopoietic growth factors
  - Fear of costs or reimbursement issues
  - Bad experience
  - "Don't think it's necessary."
  - "Would rather wait and see."
  - Do not "buy into RDI" concept.
- Patient's physical condition
  - Too weak, too tired
- Patient's negative response to prior doses
  - Extreme nausea
  - Severe drop in blood counts
  - Weight loss
- No apparent reason given by office or physician
  - Counts within "normal" range, no weight loss
  - "I think she [the patient] may not tolerate this dose."

Figure 5. Reasons for Dose Delays and Reductions Based on Fourth Quarter Data

increased RDI educational opportunities have been incorporated into chemotherapy courses and unit orientation of all interdisciplinary team members.

Two additional RDI-focused actions have been notifying physicians of chemotherapy visit cancellations and supplementing the nursing assessment form with screening criteria for the appropriate use of hematopoietic growth factors and a procedure for recommending their use to physicians. The use of hematopoietic growth factors likely will continue to escalate in light of the interim results of the Cancer and Leukemia Group B 9741 trial (Citron et al., 2003) that support a disease-free survival benefit for dose-dense versus conventional adjuvant chemotherapy for breast cancer as well as evolving practice patterns such as substituting cisplatin with carboplatin, which has a better toxicity profile overall but is more myelotoxic, in some platinum-based regimens (Desoize & Madoulet, 2002). Neutropenia is the myelotoxicity that has received the most attention from a management standpoint, which is, in part, a result of the U.S. Food and Drug Administration approval of the granulocyte colony-stimulating factor in 1991 and published clinical practice guidelines (Ozer et al., 2000); however, the prevalence and clinical significance of anemia and thrombocytopenia in patients with cancer increasingly have become appreciated in recent years (Cairo, 2000; Cunningham, 2003; Groopman & Itri, 1999; Harrison, Shasha, & Homel, 2002; Nirenberg, 2003). With the availability of newer recombinant growth factors for managing anemia (i.e., epoetin alfa or darbepoetin alfa) and thrombocytopenia (i.e., oprelvekin), clinicians now have options beyond dose delay or reduction, red blood cell or platelet transfusions associated with well-known risks and shortcomings (Rodgers et al., 2005; Schiffer et al., 2001), or no intervention while continuing chemotherapy. During the 1990s, placebo-controlled trials demonstrated that epoetin alfa and oprelvekin can be administered safely during chemotherapy to maintain or increase the hematocrit and platelet count, respectively, with a corresponding reduction in the proportion of patients requiring red blood cell and platelet transfusions, respectively (Abels, 1992; Isaacs et al., 1997; Tepler et al., 1996). Evidence is accumulating that the benefits of these recombinant growth factors extend beyond their hematopoietic effects. For example, oprelvekin was shown to reduce the rate of bacteremia of gastrointestinal origin in patients undergoing chemotherapy for hematologic malignancy, suggesting that it may confer cytoprotection or immunomodulation in the gastrointestinal epithelium (Ellis et al., 2003).

The data derived from the performance improvement initiative and ongoing nursing research study have several practical meanings. First, current methods of chemotherapy administration with regard to scheduling, how patients are scheduled, how patients cancel or reschedule, who takes the calls for cancellation, whether physicians are notified of cancellations, and reasons for cancellations must be evaluated. Second, patients, nurses, and physicians would benefit greatly from annual education on concepts related to maintaining relative dose intensity, such as (a) assessing chemotherapy-related toxicities before and during treatment to minimize dose reductions and delays, (b) accurate tracking of blood counts noting trends, (c) the appropriate use of all commercially available hematopoietic growth factors, and (d) the advantages of preventing versus managing myelosuppression. Because patients with cancer want to be cured, with most willing to do almost anything to achieve that goal, healthcare providers should initiate discussions about the premise for keeping all appointments, how patients can help themselves achieve better outcomes, and ways of resolving scheduling conflicts and securing transportation to treatment appointments.

In terms of the current status of the targeted improvement of RDI, the data collection sheet has been revised to include further detail concerning dosing and final RDI calculation (see Figure 6). Individual physicians are provided with continued targeted improvement data, including the number of patients studied, number of chemotherapy delays and dose reductions, calculation of actual RDI, and number of patients who underwent reduced or delayed chemotherapy but did not receive hematopoietic growth factors. Most of the oncology staff now agrees that every preventive measure, no matter how small, has an impact on the overall survival of patients with cancer, and concentrated efforts in improving patients' RDI will continue indefinitely.

Author Contact: Cheryl Lenhart, BSN, HRM, can be reached at clenhart@wpahs.org, with copy to editor at rose_mary@earthlink.net.

Patient:	Medical Record #	Protocol:										de novo ☐ relapsed ☐
CYCLE / DATE												
DAY OF WEEK												
BLOOD COUNT												
WHITE BLOOD CELL												
PLATELET												
HEMOGLOBIN												
HEMATOCRIT												
ABSOLUTE NEUTROPHIL COUNT												
GROWTH FACTOR GIVEN												
ARANESP®/PROCRIT® DOSE												
NEUPOGEN® DOSE												
NEULASTA® DOSE												
NEUMEGA® DOSE												
OTHER												
BLOOD / PLATELET TRANSFUSION AMOUNT												
PLANNED PER SESSION DOSE												
PLANNED TOTAL DOSE												
PLANNED TIME TO COMPLETE THERAPY (weeks)												
PLANNED DOSE INTENSITY												
ACTUAL DOSE ADMINISTERED												
ACTUAL TIME TO COMPLETE THERAPY (weeks)												
DELIVERED DOSE INTENSITY												
RELATIVE DOSE INTENSITY												
CYCLE DELAYED DUE TO MYELOSUPPRESSION		☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes
DOSE *REDUCED* DUE TO MYELOSUPPRESSION		☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes
NEW CHEMOTHERAPY DOSE												
CHANGE IN CHEMOTHERAPY AGENT		☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes
IF YES, REASON												
VISIT CANCELLED		☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes	☐ Yes
REASON FOR CANCELLATION												
PERSON CANCELLING VISIT												

Figure 6. The Western Pennsylvania Hospital Planned Dose On-Time Worksheet

Note. Reprinted with permission from the Western Pennsylvania Hospital.

Note. Aranesp®, Neupogen®, and Neulasta®; Procrit®; and Neumega® are manufactured by Amgen Inc. (Thousand Oaks, CA), Ortho Biotech Products, Inc. (Bridgewater, NJ), and Wyeth Pharmaceuticals Inc. (Philadelphia, PA), respectively.

References

Abels, R.I. (1992). Recombinant human erythropoietin in the treatment of the anaemia of cancer. *Acta Haematologica, 87*(Suppl. 1), 4–11.

Bonadonna, G., Valagussa, P., Moliterni, A., Zambetti, M., & Brambilla, C. (1995). Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer: The results of 20 years of follow-up. *New England Journal of Medicine, 332,* 901–906.

Budman, D.R., Berry, D.A., Cirrincione, C.T., Henderson, I.C., Wood, W.C., Weiss, R.B., et al. (1998). Dose and dose intensity as determinants of outcome in the adjuvant treatment of breast cancer. The Cancer and Leukemia Group B. *Journal of the National Cancer Institute, 90,* 1205–1211.

Cairo, M.S. (2000). Dose reductions and delays: Limitations of myelosuppressive chemotherapy. *Oncology, 14*(9, Suppl. 8), 21–31.

Citron, M.L., Berry, D.A., Cirrincione, C., Hudis, C., Winer, E.P., Gradishar, W.J., et al. (2003). Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741. *Journal of Clinical Oncology, 21,* 1431–1439.

Cunningham, R.S. (2003). Anemia in the oncology patient: Cognitive function and cancer. *Cancer Nursing, 26*(6, Suppl.), 38S–42S.

Desoize, B., & Madoulet, C. (2002). Particular aspects of platinum compounds used at present in cancer treatment. *Critical Reviews in Oncology and Hematology, 42,* 317–325.

Ellis, M., Zwaan, F., Hedstrom, U., Poynton, C., Kristensen, J., Jumaa, P., et al. (2003). Recombinant human interleukin 11 and bacterial infection in patients with [correction of] haematological malignant disease undergoing chemotherapy: A double-blind placebo-controlled randomised trial. *Lancet, 361,* 275–280.

Epelbaum, R., Haim, N., Ben-Shahar, M., Ron, Y., & Cohen, Y. (1988). Dose-intensity analysis for CHOP chemotherapy in diffuse aggressive large cell lymphoma. *Israel Journal of Medical Sciences, 24,* 533–538.

Frasci, G. (2002). Treatment of breast cancer with chemotherapy in combination with filgrastim: Approaches to improving therapeutic outcome. *Drugs, 62*(Suppl. 1), 17–31.

Frei, E., III, & Canellos, G.P. (1980). Dose: A critical factor in cancer chemotherapy. *American Journal of Medicine, 69,* 585–594.

Groopman, J.E., & Itri, L.M. (1999). Chemotherapy-induced anemia in adults: Incidence and treatment. *Journal of the National Cancer Institute, 91,* 1616–1634.

Harrison, L.B., Shasha, D., & Homel, P. (2002). Prevalence of anemia in cancer patients undergoing radiotherapy: Prognostic significance and treatment. *Oncology, 63*(Suppl. 2), 11–18.

Isaacs, C., Robert, N.J., Bailey, F.A., Schuster, M.W., Overmoyer, B., Graham, M., et al. (1997). Randomized placebo-controlled study of recombinant human interleukin-11 to prevent chemotherapy-induced thrombocytopenia in patients with breast cancer receiving dose-intensive cyclophosphamide and doxorubicin. *Journal of Clinical Oncology, 15,* 3368–3377.

Kwak, L.W., Halpern, J., Olshen, R.A., & Horning, S.J. (1990). Prognostic significance of actual dose intensity in diffuse large-cell lymphoma: Results of a tree-structured survival analysis. *Journal of Clinical Oncology, 8,* 963–977.

Nirenberg, A. (2003). Managing hematologic toxicities: Novel therapies. *Cancer Nursing, 26*(6, Suppl.), 32S–37S.

Norton, L. (1988). A Gompertzian model of human breast cancer growth. *Cancer Research, 48*(24, Pt. 1), 7067–7071.

Ozer, H., Armitage, J.O., Bennett, C.L., Crawford, J., Demetri, G.D., Pizzo, P.A., et al. (2000). 2000 update of recommendations for the use of hematopoietic colony-stimulating factors: Evidence-based, clinical practice guidelines. American Society of Clinical Oncology Growth Factors Expert Panel. *Journal of Clinical Oncology, 18,* 3558–3585.

Pettengell, R., Gurney, H., Radford, J.A., Deakin, D.P., James, R., Wilkinson, P.M., et al. (1992). Granulocyte colony-stimulating factor to prevent dose-limiting neutropenia in non-Hodgkin's lymphoma: A randomized controlled trial. *Blood, 80,* 1430–1436.

Rodgers, S.M., Cella, D., Chanan-Khan, A., Cleeland, C., Coccia, P.F., Demetri, G.D., et al. (2005). *Cancer and treatment-related anemia.* Retrieved December 1, 2003, from http://www.nccn.org/professionals/physician_gls/PDF/anemia.pdf

Schiffer, C.A., Anderson, K.C., Bennett, C.L., Bernstein, S., Elting, L.S., Goldsmith, M., et al. (2001). Platelet transfusion for patients with cancer: Clinical practice guidelines of the American Society of Clinical Oncology. *Journal of Clinical Oncology, 19,* 1519–1538.

Tepler, I., Elias, L., Smith, J.W., II, Hussein, M., Rosen, G., Chang, A.Y., et al. (1996). A randomized placebo-controlled trial of recombinant human interleukin-11 in cancer patients with severe thrombocytopenia due to chemotherapy. *Blood, 87,* 3607–3614.