

# Assessment of Neutropenia-Related Quality of Life in a Clinical Setting

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**Purpose/Objectives:** To examine how neutropenia affects quality of life (QOL) and explore strategies to assess neutropenia-related QOL in clinical practice.

**Data Sources:** Published articles, abstracts, conference proceedings, and clinical practice guidelines.

**Data Synthesis:** Neutropenia can have a detrimental effect on the QOL of patients receiving chemotherapy. A neutropenia-related QOL questionnaire can help nurses better identify patients at risk for developing neutropenia and monitor patients who already have it. In some cases, the questionnaire may be the first step in the initiation of interventions to improve patient care. Ideally, the QOL questionnaire should be easy to use, provide clinically meaningful information, and be easily adapted from existing QOL measurement tools.

**Conclusions:** Effective implementation of QOL assessments into clinical practice can lead to the initiation of interventions that may improve neutropenia-related QOL in patients with cancer receiving chemotherapy.

**Implications for Nursing:** Nurses can enhance their clinical judgment and affect patient treatment by implementing a questionnaire that assesses patients' neutropenia-related QOL.

Quality of life (QOL) is a multidimensional concept that assesses the extent to which a person's usual or expected physical, emotional, and social well-being is affected by a medical condition or its treatment (Cella, Chang, Lai, & Webster, 2002). QOL, symptom status, and functional status frequently are considered to be interchangeable, but they represent three related but ultimately distinct concepts (Ropka, 2002). Symptom status refers to a patient's experience of physical, emotional, or cognitive manifestations of illness or treatment, such as nausea, anxiety, or confusion. Functional status refers to the effect of illness or treatment on a patient's ability to perform day-to-day tasks involved in work, self-care, and maintenance of family or social roles. QOL, which encompasses symptom status and functional status, is a broad concept reflecting an individual's overall satisfaction with life or sense of well-being (Ropka). QOL endpoints for cancer treatments increasingly are recognized as secondary in importance only to survival and disease progression. In the palliative setting, QOL outcomes are paramount (American Society of Clinical Oncology, 1996; Levine & Ganz, 2002; Sloan, Cella, Frost, Guyatt, & Osoba, 2003). Clinical questionnaires to evaluate QOL are used widely in oncology nursing practice because of their value in guiding patient treatment and care (Dunckley, Hughes, Addington-Hall, & Higginson, 2003). In this context, the term "instrument" generally refers to a questionnaire in which patients answer questions about symptoms, functioning, or feelings, often stating answers in a numerical or graded form (e.g., expressing the intensity of pain on a scale of 0–10 or as mild, moderate, or severe).

## Key Points . . .

- ▶ Because the development of neutropenia and its associated reduction in quality of life (QOL) can affect treatment outcomes in patients with cancer receiving chemotherapy, healthcare professionals should assess such patients' QOL before the initiation of therapy and periodically throughout treatment.
- ▶ Several QOL measurement tools are available and widely used in research, but they may not be suitable for clinical practice.
- ▶ Customizing QOL measurement tools can make them more user friendly, practice specific, and clinically useful.
- ▶ Implementation of a QOL screening questionnaire for neutropenia could help nurses identify at-risk patients and guide interventions that could have a positive influence on patients' treatments.

Neutropenia (grade 3/4, absolute neutrophil count [ANC]  $< 1.0 \times 10^9/L$ ) is a common and serious side effect of myelosuppressive chemotherapy and may lead to febrile neutropenia (ANC  $< 1.0 \times 10^9/L$ , fever  $< 38.5^\circ C$ ) and life-threatening infections (Cancer Therapy Evaluation Program, 2003; Daniel & Crawford, 2006). Furthermore, chemotherapy-induced neutropenia frequently compromises the delivery of chemotherapy at full dose and on schedule (Picozzi et al., 2001). Delivery of suboptimal doses of chemotherapy may compromise long-term survival in potentially curative settings, such as early-stage breast cancer and non-Hodgkin lymphoma (Bonadonna et al., 2005; Epelbaum, Haim, Ben-Shahar, Ron, & Cohen, 1988; Kwak, Halpern, Olshen, & Horning, 1990). Studies also have shown that alterations in chemotherapy regimens may worsen treatment outcomes in patient populations in which treatment is less commonly curative, such as small cell lung cancer (Crawford, 2004). Although the benefits of myelosuppressive chemotherapy often outweigh the threats posed by neutropenia-related consequences, treatments can decrease the risk of neutropenia (Daniel & Crawford). Precautionary measures to reduce the

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risk of infection and complications are imperative in patients receiving myelosuppressive chemotherapy; however, some of the measures may adversely affect patients' QOL (Lyman & Kuderer, 2002; Padilla & Ropka, 2005).

To date, only a few studies have used a validated QOL questionnaire to assess the effect of neutropenia on QOL (Calhoun, Chang, Welshman, & Cella, 2002, 2003; Fortner et al., 2002; Okon et al., 2002). Available data from the studies show that deficits in QOL are associated with ANC nadir and neutropenia-related chemotherapy delays (Calhoun et al., 2002, 2003; Fortner et al., 2002; Okon et al.). A validated, neutropenia-specific QOL questionnaire designed for use in nursing practice is not yet available but would be an asset to guiding treatment interventions and patient care. This review describes the importance of measuring neutropenia-related QOL and discusses the attributes of a neutropenia-related QOL questionnaire that could be implemented in clinical practice. The terms "research" and "practice," as used in this article, refer to clinical research and clinical practice, respectively.

## **Rationale for Measuring Neutropenia-Related Quality of Life in Practice**

Patients with neutropenia may experience deficits in QOL for a number of reasons (Lyman & Kuderer, 2002). Because they are more susceptible to infection, patients with neutropenia can be taught to take extra precautions, such as avoiding crowds, maintaining a low-microbial diet, and routinely monitoring for breaks in the skin or oral mucositis (Larson & Nirenberg, 2004). Because of the serious medical consequences associated with febrile neutropenia, patients with the condition typically are hospitalized and subject to invasive diagnostic and treatment procedures such as IV antibiotics. To minimize opportunities to contract infections, such patients may be separated from friends, family, and the home environment for prolonged periods, during which their normal social and work routines are put on hold. Data from a retrospective study suggest a trend toward greater incidence, duration, and severity of other common chemotherapy toxicities in patients with breast cancer who develop severe neutropenia (ANC < 0.5 x 10<sup>9</sup>/L) compared to patients who do not. The incidence and severity of toxicities were markedly greater (two- to fivefold) during the period in which febrile neutropenia occurred than in patients who did not experience febrile neutropenia (Glaspy, Hackett, Flyer, Dunford, & Liang, 2001).

Clinical research shows that QOL at baseline may be an independent predictor of survival in several tumor types (Dancey et al., 1997; Hwang et al., 2004; Kramer et al., 2000; Maisey et al., 2002; Montazeri, Milroy, Hole, McEwen, & Gillis, 2001; Roychowdhury, Hayden, & Liepa, 2003). Furthermore, poor QOL during chemotherapy treatment may affect patients' ability or willingness to complete treatment (Cella et al., 2002). Therefore, when developing treatment plans, healthcare professionals should take QOL into consideration, along with other clinical factors.

QOL measurements can be used during clinical encounters to screen for potential problems and facilitate dialogue

among patients, families, caregivers, and healthcare professionals. A QOL questionnaire can address social and psychological problems that otherwise may be overlooked unless patients are specifically asked about them. A QOL questionnaire can be used by staff members and patients before or after chemotherapy-related complications to help identify, prioritize, and develop strategies for treatment. Getting patients involved in making decisions about treatment may be useful because compliance with therapy may be poor if patients do not perceive that treatments are achieving the improvements, changes, or goals that they expect (Higginson & Carr, 2001).

Health-related QOL assessment also can be incorporated into clinical decision making with respect to intervention. Results can be used to determine whether a particular treatment should be initiated or discontinued or whether alternatives should be considered. In many clinical situations, evaluating the efficacy of cancer treatments by tumor response or survival is inadequate, and laboratory tests alone are not sufficient to monitor patients' perceptions of their responses to treatments (Crighton, 2004). The underlying reason for using QOL measurement tools in practice is to ensure that treatment plans and evaluations focus on the patient rather than on the disease (Higginson & Carr, 2001).

The use of QOL measurement tools in practice differs from their use in research. In cancer treatment trials in which survival is the primary outcome, measurement of QOL can differentiate among treatments with equivalent survival rates (Goodwin, Black, Bordeleau, & Ganz, 2003). In symptom management trials, QOL measurement tools are used to correlate patient-reported symptom relief and global improvements in QOL (Buchanan, O'Mara, Kelaghan, & Minasian, 2005). The qualities required in research for QOL measurement are, despite some overlap, relatively distinct from those required for use in practice.

## **Measurement of Neutropenia-Related Quality of Life**

One of the biggest challenges of QOL assessment is deciding which QOL questionnaire is the most relevant to use in each clinical situation (Sloan et al., 2003). Because health-related QOL is multidimensional and must be evaluated by patient self-assessment, its measurement remains complex. More than 500 general or targeted health-related QOL instruments have been developed (MAPI Research Institute, 2006). General QOL questionnaires ask broad questions and are useful in conducting survey research on overall health and in comparing different diseases. One such questionnaire is the European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire-C30 (EORTC QLQ-C30), a widely used 30-item instrument that detects depression, anxiety, symptom burden, and functional limitation in patients receiving treatment for a wide variety of cancers (Sprangers, Cull, Bjordal, Groenvold, & Aaronson, 1993). Targeted QOL questionnaires that are disease specific or condition specific are sensitive to changes in certain patient populations and are more useful in clinical trials in which therapeutic interventions are being evaluated (Cella et al., 2002). The Functional Assessment of Cancer Treatment (FACT) is a targeted instrument that has been validated in patients with cancer and used for more than a decade (Cella et al., 1993). The FACT includes a

general questionnaire (FACT-G), as well as several validated disease-, treatment-, and symptom-specific subscales, such as FACT-Fatigue and FACT-Anemia (Yellen, Cella, Webster, Blendowski, & Kaplan, 1997).

A variety of QOL questionnaires, both general and cancer specific, have been used in studies to explore the effect of neutropenia on QOL in patients undergoing myelosuppressive chemotherapy (see Table 1). In a prospective, observational, single-center study, several instruments were used to evaluate QOL in 62 patients with a variety of cancer types who were treated with chemotherapy but not proactive growth factors (Fortner et al., 2002). The most common tumor sites were lung (37%) and breast (16%); 63% of patients were characterized as having advanced disease. Approximately 50% of patients experienced grade 4 neutropenia, and they had a greater decline in QOL scores from baseline to ANC nadir than patients without grade 4 neutropenia. Physical aspects of QOL were most compromised, with significant increases in the bodily pain and general physical symptoms items on the Cancer Care Monitor (CCM) and in the treatment-related side effects item on the Short Form-36 (SF-36) Health Survey used in the Medical Outcomes Study (Fortner et al., 2002). The Hospital Anxiety Depression Scale and the Psychosocial Adjustment to Illness Scale also were used but did not detect significant differences.

Deficits in QOL correlated with lower ANC in a retrospective study of 44 patients with a variety of cancer types and grade 4 chemotherapy-induced neutropenia. The patients were identified from a community clinical database that contained ANC counts and results of the CCM. Patients reported a variety of symptoms, the most frequent being fatigue (91%) and impairment in normal functioning or performance of activities of daily living (89%). Lower ANC was significantly correlated with a decreased ability to perform light or hard physical work ( $p < 0.05$  for each) and reduced normal functioning ( $p < 0.01$ ). The study also found that lower ANC was asso-

ciated with decreased global QOL ( $p < 0.05$ ) and impaired performance ( $p < 0.01$ ) (Okon et al., 2002). However, because the Fortner et al. (2002) and the Okon et al. studies included only a small proportion of patients who developed febrile neutropenia, their results may be best interpreted in the context of severe afebrile neutropenia.

Five questionnaires were used in parallel to evaluate the effect of neutropenia-induced dose delays on the QOL and mood of 140 newly diagnosed patients receiving chemotherapy (Calhoun et al., 2003). Of those patients, 56% had been diagnosed with breast cancer and 25% with ovarian cancer. Compared with patients who did not experience delays, the 18 patients who did experience delays exhibited significant increases from baseline in intrusive and avoidant thoughts on the Impact of Events Scale ( $p = 0.001$ ) and tension ( $p = 0.0001$ ), depression ( $p = 0.04$ ), and anger ( $p = 0.035$ ) on the Profile of Mood States. Other scales, including the FACT-G, did not detect significant differences between those who experienced delays in chemotherapy administration and those who did not (Calhoun et al., 2003).

Calhoun et al. (2002) developed a neutropenia-specific subscale of the FACT (FACT-N) that contains 19 items in addition to the 27 items on the FACT-G (see Figure 1). Patients use a five-point rating system, from 0 (not at all) to 4 (very much), to produce a composite score in addition to individual scores for the domains of physical, functional, social, emotional, and neutropenia-related well-being (Calhoun et al., 2002; Cella et al., 1993). Studies indicate that FACT subscales for neutropenia or neuropathy may be able to detect differences in QOL in patients with cancer where the FACT-G does not (Calhoun et al., 2002). Tests to further evaluate the FACT-N's validity, reliability, and sensitivity to clinical change are ongoing. In the future, the FACT-N questionnaire could be used to assess outcomes in clinical studies or as a questionnaire to guide the clinical management of chemotherapy-induced neutropenia (Calhoun et al., 2002).

**Table 1. Quality-of-Life Instruments Used to Measure Neutropenia-Related Quality of Life in Patients With Cancer**

Instrument	Targets General Health-Related Quality of Life	Is Cancer Specific	Is Symptom Specific	Web Site
Cancer Care Monitor (Fortner et al., 2003)	–	X	–	<a href="http://westclinic.com">http://westclinic.com</a>
Functional Assessment of Cancer Treatment–Fatigue (Yellen et al., 1997)	–	–	X	<a href="http://www.facit.org">www.facit.org</a>
Functional Assessment of Cancer Treatment–General (Cella et al., 1993)	–	X	–	<a href="http://www.facit.org">www.facit.org</a>
Functional Assessment of Cancer Treatment–Neutropenia (Calhoun et al., 2002)	–	–	X	<a href="http://www.facit.org">www.facit.org</a>
Functional Living Index–Cancer (Cheung et al., 2004)	–	X	–	Not available
Hospital Anxiety and Depression Scale (Bjelland et al., 2002; Zigmond & Snaith, 1983)	X	–	–	Not available
Impact of Events Scale (Calhoun et al., 2003)	X	–	–	<a href="http://www.mardihorowitz.com/works.htm">www.mardihorowitz.com/works.htm</a>
Profile of Mood States (Calhoun et al., 2003; Goodwin et al., 2003)	X	–	–	<a href="http://www.mhs.com">www.mhs.com</a>
Psychosocial Adjustment to Illness Scale (Fortner et al., 2002)	X	–	–	<a href="http://www.derogatis-tests.com">www.derogatis-tests.com</a>
Short Form-36 (Ware et al., 1996)	X	–	–	<a href="http://www.sf-36.org">www.sf-36.org</a>
Spielberger State-Trait Anxiety Inventory (Calhoun et al., 2003; Goodwin et al., 2003)	X	–	–	Not available

Below is a list of statements that other people with your illness have said are important. By circling one number per line, please indicate how true each statement has been for you during the past seven days.

	<u>Not at all</u>	<u>A little bit</u>	<u>Somewhat</u>	<u>Quite a bit</u>	<u>Very much</u>
1. I worry about getting sick due to low blood counts.	0	1	2	3	4
2. I avoid public places for fear of getting an infection.	0	1	2	3	4
3. I get aches and pains that bother me.	0	1	2	3	4
4. I need help doing my usual activities.	0	1	2	3	4
5. I worry about infections.	0	1	2	3	4
6. I worry that my condition will not improve if my treatment is delayed.	0	1	2	3	4
7. I have energy.	0	1	2	3	4
8. I am bothered by fevers.	0	1	2	3	4
9. I am bothered by chills.	0	1	2	3	4
10. I have night sweats.	0	1	2	3	4
11. I have to limit my social activity because I am tired.	0	1	2	3	4
12. I need to rest during the day.	0	1	2	3	4
13. I feel listless ("washed out").	0	1	2	3	4
14. I am motivated to do my usual activities.	0	1	2	3	4
15. I have mouth sores.	0	1	2	3	4
16. My partner worries about me when my blood counts are low.	0	1	2	3	4
17. My low blood counts interfere with my intimate relationships.	0	1	2	3	4
18. I have trouble starting things because I am tired.	0	1	2	3	4
19. I am bothered by headaches.	0	1	2	3	4

**Figure 1. The Neutropenia Subscale of the Functional Assessment of Cancer Treatment**

*Note.* From *A Neutropenia-Specific Quality of Life Instrument: Rationale for the Development of the FACT-N* [Abstract 1498], by E.A. Calhoun, C.H. Chang, E. Welshman, and D. Cella, May 2002, poster presented at the annual meeting of the American Society of Clinical Oncology, Orlando, FL. Copyright 2002 by the American Society of Clinical Oncology. Reprinted with permission.

## Design and Implementation of Quality-of-Life Measurement Tools in Practice

Existing instruments have been used to measure neutropenia-related QOL in research thus far but may not be readily implemented in practice. Time and budgetary constraints often differ in clinical trials compared with routine practice; some QOL instruments may take as long as 30 minutes to administer and require extensive staff training. Furthermore, QOL questionnaires used in clinical trials are applicable to large samples, and scores often are presented as means. Such scores may be useful when comparing one treatment against another in groups of patients but are less helpful in practice where the information is used as a basis for clinical decisions regarding individual patients. The questionnaires may need to be calibrated and thresholds defined to determine when the problem is considered to be severe or to require intervention (Higginson & Carr, 2001). Figure 2 provides a list of desirable features for a neutropenia-related QOL questionnaire that is intended for use in regular practice.

QOL questionnaires used in research and practice should be valid and reliable (Cella et al., 2002; Higginson & Carr, 2001). Results should be reproducible when a questionnaire is administered by different individuals (inter-rater reliability) and on different occasions (test-retest reliability) when the QOL being measured is stable. A questionnaire must measure what it is intended to measure and be sensitive to clinically meaningful change. Clinicians should be aware of the QOL questionnaire and be convinced that the information derived from the questionnaire can lead to further action that may improve patient care. Ideally, QOL measurement tools should be inexpensive, quick to complete, simple to understand, and not an additional burden for patients or staff (Ballatori, 2001). These qualities

are illustrated in the one-item numerical rating scale of cancer pain, where patients are asked to write down, circle, or state their level of pain intensity from 0–10 (Jensen, 2003).

A growing amount of research has focused on making QOL questionnaires easier to use. Researchers have developed computer-administered questionnaires, such as the CCM, Pain Intensity Numerical Scale (PINS), Symptom Distress Scale (SDS), and Short Form-8 (SF-8), and initial evaluations suggest that the questionnaires are feasible, valid, and reliable (Berry et al., 2004; Fortner, Okon, Schwartzberg, Tauer, & Houts, 2003). An acceptability survey conducted in 45 patients who completed computerized versions of the PINS, SDS, and SF-8 showed that a majority of patients found the program easy to use (79%), easy to understand (91%), and enjoyable (71%). Most of the 12 clinicians involved in the study found that the generated information was useful for promoting communication with patients, identifying patients' QOL concerns, and guiding clinical interventions (Mullen, Berry, & Zierler, 2004).

Established QOL measurements also have been simplified to be more usable in the clinical setting without losing accuracy (Chang, Hwang, Kasimis, & Thaler, 2004; Cheung et al., 2004; Ware, Kosinski, & Keller, 1996). For example, Ware et al. altered the SF-36, removing 24 of the 36 items with minimal loss in measurement precision. Chang et al. successfully streamlined the Memorial Symptom Assessment Scale, scaling back from 32 symptoms to 14 key symptoms that provide the majority of prognostic information, reducing completion time from 5–10 minutes to 2–4 minutes. A shortened Chinese version of the Functional Living Index–Cancer (FLIC) questionnaire was developed and named Quick-FLIC; it was shown to provide valid and reliable measurements of QOL (Cheung et al.). Although the reliability and validity of many of the QOL instruments have been demonstrated in clinical

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**Accessible:** usable across a wide range of patient literacy levels

**Culturally appropriate:** culturally sensitive and in an optimal language for the patient population

**Easy patient use:** simple, easy to understand, and quick to use

**Easy staff use:** quick to use and easy to score and interpret results; requires minimal staff training

**High sensitivity:** detects changes in patient quality-of-life (QOL) status that are clinically relevant; does not produce false negatives

**High specificity:** detects QOL changes that are rooted in actual clinical changes; does not produce false positives

**Records compatible:** produces results that are incorporated easily into patient medical records

**Reliable:** generates QOL scores that are reproducible from occasion to occasion given no other significant changes in the patient and that are similar between healthcare providers evaluating the same patient at the same point in time

**Targeted:** specifically designed to assess the QOL, symptom, and functional impacts of neutropenia

**Valid:** produces results that reflect QOL in a wide range of patients with a wide range of tumor sites, stages, and treatment regimens

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### **Figure 2. Desirable Characteristics for a Questionnaire Measuring Neutropenia-Related Quality of Life in Clinical Practice**

trials, further studies are required to evaluate their routine use in practice (Higginson & Carr, 2001).

Clinical experience indicates that challenges may arise when implementing new QOL questionnaires, including staff acceptance (Higginson & Carr, 2001). The evidence base behind the development of a QOL instrument and the benefits of using a questionnaire should be demonstrated clearly. A program to train staff in the use of the QOL questionnaire and in the interpretation of results should be developed and implemented to guide treatment interventions. Ideally, practice guidelines should be revised to incorporate QOL measurements, and QOL results should be included in clinical records.

Cultural differences in a clinic's patient population may affect the interpretation of results from a QOL instrument (Aaronson, 1998; Cella et al., 1998, 2002; Dunckley et al., 2003; Lubeck et al., 2001). Healthcare professionals should consider the influence that culture and religion may have on concepts about disease, illness, and mood states such as depression. Translating a QOL questionnaire while maintaining cross-cultural relevance, equivalence, and meaning remains a significant challenge (Dunckley et al.). Communication that can tie cultural and religious influences into the clinical judgment of healthcare professionals is paramount when selecting and administering a QOL questionnaire in practice.

## **Application of a Neutropenia-Related Quality-of-Life Questionnaire in Practice**

Application of a neutropenia-related QOL questionnaire in clinical practice may improve communication between patients and physicians (Higginson & Carr, 2001) and lead to action that may improve survival (Dancey et al., 1997; Hwang et al., 2004; Kramer et al., 2000; Maisey et al., 2002; Montazeri et

al., 2001; Roychowdhury et al., 2003). Ideally, a QOL questionnaire should be brief and easy to use and should enhance discussions about QOL between physicians and patients. A QOL questionnaire can be a platform for physicians and patients to develop plans to address QOL-related problems with possible interventions, such as stress counseling or help with caregiving. Evidence-based risk models may permit the identification of patients at high risk for neutropenic complications (Ropka, Padilla, & Gillespie, 2005), but results of a QOL questionnaire should be considered when identifying appropriate intervention.

Other management options for chemotherapy-induced neutropenia include proactive dose reductions or dose reductions or treatment delays after neutropenic complications have occurred. Both strategies have the disadvantage of reducing chemotherapy dose intensity, which could seriously compromise treatment outcomes in settings where cure or disease-free survival is the goal of treatment (Bonadonna et al., 2005). Proactive administration of granulocyte colony-stimulating factor (G-CSF) as an adjunct to myelosuppressive chemotherapy can reduce the incidence and severity of neutropenia, hospitalizations, and IV antibiotic use resulting from infections (Daniel & Crawford, 2006). Proactive use of G-CSF can manage risk of infection without reducing chemotherapy dose intensity, as demonstrated in a meta-analysis of 14 controlled trials of G-CSF in which the average delivered chemotherapy dose intensity was significantly greater in patients who received G-CSF ( $n = 2,483$ ) than in control patients ( $n = 1,574$ ) (95% versus 88%,  $p < 0.001$ ) (Kuderer, Crawford, Dale, & Lyman, 2005). Even in the palliative setting, where dose attenuation may be appropriate, reducing the risk of infection and related QOL deficits is preferable to managing infections after they have occurred. Furthermore, dose delays have been observed to negatively affect QOL, causing significant increases in intrusive and confused thoughts (Calhoun et al., 2003).

One study reported that the proactive use of G-CSF reduces symptom burden and improves health-related QOL. In patients with node-negative breast cancer, QOL, as measured by the EORTC QLQ-C30 scale, was worse in patients treated with adjuvant docetaxel, doxorubicin, and cyclophosphamide (TAC) when compared to those treated with fluorouracil, doxorubicin, and cyclophosphamide. However, when G-CSF was used in the first and subsequent cycles along with the TAC regimen, no difference in QOL was observed; the addition of G-CSF to TAC correlated with a reduction in the incidence of febrile neutropenia, severe diarrhea, asthenia, and oral mucositis compared to TAC alone (Martin et al., 2005). In addition to demonstrating the potential effectiveness of proactive G-CSF for improving QOL, the study demonstrated the correlation between health-related QOL measured by a questionnaire and rates of tangible, clinically evaluable adverse events (see Table 2).

Evidence-based guidelines published by the National Comprehensive Cancer Network (2007) recommend proactive use of G-CSF in patients with cancer at high risk (> 20%) for developing febrile neutropenia or other neutropenic complications that could compromise dose intensity. In addition, the guidelines also recommend that G-CSF be considered for improved QOL and symptom management when patients are at high or intermediate risk for febrile neutropenia. Nurses should assess for neutropenia in all patients about to undergo myelosuppressive chemotherapy and evaluate the risk of the prescribed chemotherapy regimen in addition to factors that increase patients' risk of infection, such as older age and comorbid conditions (National Comprehensive

**Table 2. Neutropenia, Health-Related QOL, and Clinically Evaluable Adverse Events in TAC-Treated Patients Receiving or Not Receiving Proactive G-CSF**

Variable	TAC + G-CSF (%) (N = 416)	TAC Alone (%) (N = 114)	p
Patients exhibiting > 10-point decrease in health-related QOL following cycle 6 <sup>a</sup>	45.6	64.0	0.0233
Febrile neutropenia	6.5	24.6	< 0.001
Asthenia	5.6	20.2	< 0.0001
Stomatitis (grade 2–4)	23.2	35.0	0.01
Diarrhea	2.7	7.0	0.02
Myalgia	0.2	2.6	0.03
Discontinuation because of adverse event	2.9	7.9	NE
Proportion of cycles with dose reduction	2.2	4.7	NE

<sup>a</sup>As assessed by European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire-C30.

G-CSF—granulocyte-colony-stimulating factor; NE—not evaluated; QOL—quality of life; TAC—docetaxel, doxorubicin, and cyclophosphamide  
*Note.* Based on information from Martin et al., 2005.

Cancer Network). A neutropenia-related QOL instrument used in conjunction with an evidence-based risk assessment questionnaire (Ropka et al., 2005) could allow nurses to identify patients with unacceptable QOL deficits who also should be considered for G-CSF therapy.

Nurses are aware that frequent travel to clinics for cancer treatment and supportive care can increase the burden on patients and their caregivers and further affect QOL. Each visit disrupts normal daily routines, and travel can be logistically difficult and contribute to out-of-pocket costs (Fortner et al., 2004; Payne, Jarrett, & Jeffs, 2000). Patients may appreciate strategies to minimize the number of visits required, such as use of the longer-acting G-CSF, pegfilgrastim (Viens, De Koninck, Mercier, St-Onge, & Lorrain, 2003). One injection of pegfilgrastim provides equal protection to that provided by multiple daily injections of filgrastim (Green et al., 2003; Holmes et al., 2002). Nurses must ensure, however, that patients who receive pegfilgrastim (and therefore make fewer clinic visits) are able to self-monitor for signs and symptoms of febrile neutropenia and other chemotherapy-related toxicities (Bedell, 2003).

## Conclusion

Because neutropenia and neutropenia-related QOL deficits may affect treatment outcomes in patients with cancer receiving chemotherapy, such problems should be avoided. A neutropenia-specific QOL questionnaire that is suitable for nurses to use in routine practice should be developed. Implementation of neutropenia-related QOL screening questionnaires in practice could help nurses guide interventions that may have a positive influence on patients' treatment.

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