

# BREAST CANCER IN FOCUS

Current Developments in the Management of Breast Cancer

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## What Is the Optimal Way to Evaluate Quality of Life in Breast Cancer Trials?



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**H&O** What are the main quality-of-life issues faced by women who are being treated for breast cancer, and those who have completed treatment?

**PG** During treatment, patients are subject to numerous side effects that we are well aware of, but are not always good at treating. We are able to do a fairly good job of controlling nausea and vomiting, for example, but fatigue and psychologic distress are more difficult to treat. Another side effect that we are recognizing more often is cognitive changes during treatment. With the switch to taxanes, we also are seeing numerous patients with neuropathy and pain.

After treatment ends, certain symptoms can persist for months or years. These include fatigue, cognitive complaints, sexual dysfunction, sleep problems, and neuropathy.

**H&O** How does quality of life in breast cancer compare with that in other types of cancer?

**PG** The drugs that we use as primary treatment for breast cancer are similar to those used in other cancers, such as lung cancer, so the side effects are similar as well. A major difference between breast cancer and lung cancer, however, is that patients with breast cancer tend to have a better prognosis. Because of the high likelihood of cure, breast cancer patients are willing to put up with a lot more during treatment. They may be willing to undergo intense treatments that lead to long-term survival, but may produce persistent problems.

Another factor in breast cancer therapy is endocrine treatment, which is used by approximately 65% to 70% of women with breast cancer, sometimes in conjunction

with ovarian suppression. Women who take an aromatase inhibitor or tamoxifen usually wind up dealing with hormone-related changes, which include hot flashes, night sweats, vaginal dryness, and sometimes cognitive changes. Some women receive endocrine therapy without chemotherapy, but the women who get treated with both have far more prolonged side effects.

**H&O** How do studies traditionally measure quality of life in breast cancer?

**PG** We generally use questionnaires that look not only at symptoms, but also at functioning in 3 or 4 domains, such as physical functioning, emotional well-being, social functioning, body image, or sexual functioning. Many different questionnaires are available, so for clinical trials, we are able to choose one that fits the particular issue or side effect we are examining, whether that be depression, fatigue, or any other quality-of-life issue.

**H&O** How detailed are the questionnaires?

**PG** Some of the questionnaire batteries contain as many as 60 to 100 items.

**H&O** Does having such a long questionnaire cause problems with adherence?

**PG** Patients usually do not have any difficulty filling these out because they are waiting in the clinic anyway, so even a questionnaire that takes 15 or 20 minutes does not pose a problem. Patients are often glad that someone cares about

their experience with treatment. In the cooperative groups that I have worked with, including the National Surgical Adjuvant Breast and Bowel Project (NSABP), we generally have seen 80% to 90% adherence with completion of forms. In a 2010 study published in the *Journal of Clinical Oncology* in which we looked at sentinel node biopsy, we actually had very good adherence to patient questionnaires regarding arm function and related symptoms. In a 2011 study in the *Journal of Clinical Oncology* in which we looked at quality of life and continuation or cessation of menstruation in the NSABP B-30 trial, we found that we had a very high adherence rate with the questionnaires.

When we need to ensure that the staff members collect all the necessary data, we sometimes offer an extra \$50 per case or extra cancer-control credits. That acts as a bit of an incentive for taking the extra time to give the patient the questionnaire to complete.

### H&O Are there any newer approaches to measuring quality of life in breast cancer?

**PG** The content of the questionnaires continues to evolve over time to reflect the side effects of the agents we are using, but the biggest change is the use of electronic devices to capture the data and administer the questionnaires.

### H&O How often do breast cancer studies look at quality of life?

**PG** We spent many years looking at quality of life in the adjuvant setting, starting in the 1990s. We know that the treatments are toxic, and we know that most women recover within a year—as in the NSABP B-30 trial. Furthermore, it is hard to detect significant differences between different regimens. As a result, there is no need to measure quality of life in most trials of adjuvant chemotherapy. The exceptions would be trials of agents that appear to have an unusual toxicity or an unusually large benefit in terms of reduced toxicity or improved survival. Only in the rare instance of an equivalency trial would quality-of-life assessment be critical, because the treatment with the best quality-of-life outcomes is preferable when all other outcomes are equal. We also should measure quality of life in trials that compare conventional chemotherapy with targeted therapy, because there may be very different patterns of toxicity and patient-reported outcomes.

### H&O Has a breast cancer agent ever been approved based on quality of life?

**PG** No, not that I know of, although this has occurred in prostate cancer (with mitoxantrone) and in pancreatic cancer (with gemcitabine).

### H&O What special quality-of-life concerns exist for women with metastatic breast cancer?

**PG** One of the biggest issues for women living with metastatic disease is the anxiety that comes with being on continuous therapy and not knowing how long it will benefit them. In addition, many of the drugs that these women take are expensive, so financial toxicity can be a concern with ongoing continuous therapy. Many women are no longer able to work, which can lead to social isolation and increased financial worries. Pain and other symptoms also can occur.

### H&O What special concerns exist for younger women?

**PG** I have been actively engaged in research on younger women, who are facing a life-threatening disease at a time when people generally expect to be healthy. A 35-year-old woman with breast cancer does not have many peers who are facing such a serious illness. Hair loss and changes in body image can be especially traumatic for a young woman. A lack of interest in sex and vaginal dryness also can become a big problem for women who are married or dating. These women also may be balancing child rearing with work or education, and then cancer comes along. Younger women with a diagnosis of breast cancer tend to have a lot more psychologic distress than older women, and they can have a lot more symptoms related to premature menopause, as discussed in a 2012 review article in the *Journal of the National Cancer Institute*.

### H&O At what phase of treatment should quality of life be measured?

**PG** If we want to look at the late effects of cancer treatment, we need to test women before treatment and at intervals after treatment that go beyond 1 or 2 years.

Approximately 25% of women have ongoing difficulties that do not resolve after a year or two. Women in this group may not be able to go back to work because of substantial cognitive impairment or fatigue.

### H&O What steps should be taken to improve quality of life in women who are being treated for breast cancer?

**PG** During treatment, we need to focus on addressing both symptoms and psychosocial needs. For example, one symptom that often fails to get addressed is pain from growth factors such as filgrastim. Women may be able to tolerate the pain, but treating it is much better. We also should provide psychosocial interventions when appropriate; for example,

anxiety and depression can be very effectively managed with counseling and medications.

**H&O** What steps should be taken for women who have completed their initial treatment for breast cancer?

**PG** One of the things that happens to breast cancer survivors is that they finish their initial treatment, and then the rest of the family thinks that their health problems are all over. But as we know, it may take quite a while for certain symptoms to resolve. Just because 6 months have passed and the person's hair has grown back does not mean that everything is back to normal. Cancer survivors have a new normal, and they need to adjust to that.

This is when some women start going to support groups for the first time. They want to speak to other people who have gone through the same experience because their family may be tired of hearing about it, and their physician may not have specific advice for them.

**H&O** What else should clinicians be doing to address quality of life in their patients?

**PG** I think that just as we use precision medicine to treat the tumor with the right therapy, we should identify the problems that specific women are most likely to experience. It would be valuable to learn who might be particularly susceptible to a long-term or late effect such as neuropathy, fatigue, or cognitive difficulties, and to tailor our therapies with this in mind or intervene early to prevent

their persistence. We also should attempt to modify our therapies so that we are not overtreating people.

Another important point is that we may treat 100 women with exactly the same regimen, and see these problems in only 15% or 20% of them. Why is that? A lot of us would like to learn the answer to that question, and then learn how to tailor treatment in such a way that we could avoid giving certain kinds of treatments to women who are more vulnerable to these long-term effects.

**Suggested Readings**

Ganz PA, ed. *Improving Outcomes for Breast Cancer Survivors: Perspectives on Research Challenges and Opportunities*. New York, NY: Springer; 2015.

Ganz PA, Kwan L, Stanton AL, Bower JE, Belin TR. Physical and psychosocial recovery in the year after primary treatment of breast cancer. *J Clin Oncol*. 2011;29(9):1101-1109.

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Lemieux J, Goodwin PJ, Bordeleau LJ, Lauzier S, Théberge V. Quality-of-life measurement in randomized clinical trials in breast cancer: an updated systematic review (2001-2009). *J Natl Cancer Inst*. 2011;103(3):178-231.

**Erratum**

An interview in the July 2014 issue, “Immunoconjugates in the Treatment of Breast Cancer” with Debu Tripathy, MD, contained an incorrect figure reference because of an editing error. The correct reference is “Barok M, Joensuu H, Isola J. Trastuzumab emtansine: mechanisms of action and drug resistance. *Breast Cancer Res*. 2014;16(2):209.”