Side Effects, Quality-of-Life Issues, and Trade-offs: the Patient Perspective

Amy S. Langer

Increasingly effective adjuvant treatments of invasive breast cancer and their widespread use have improved survival rates. Given the timing required by its use, adjuvant therapy requires the patient to absorb complex medical data and make challenging trade-offs shortly after initial diagnosis. However, many women are unprepared or unable to optimize adjuvant treatment decisions while experiencing the shock and dismay that often follow the confirmation of an invasive breast cancer diagnosis. Each woman needs to know the facts and circumstances of her own case and to fully understand the benefits and risks of adjuvant therapy. Only then can she, with her medical team, choose those therapies that will maximize her benefit as a patient and as a survivor in all aspects of her life, over both the short and longer term.

To help the patient accomplish these goals, individualized practical knowledge that complements population-based advances in survival is critically needed. Considerable focus, study, and cross-disciplinary collaboration will be required to compile successful, integrated approaches to adjuvant therapy that reflect varying patient contexts and concerns. Other crucial ingredients are the investment of resources in recently established research fields (such as the tracking of psychosocial outcomes and delayed morbidity) and informed guidance from patient advocates. To accelerate patient-centered progress in adjuvant therapy for breast cancer, areas that need attention include targeted public education programs; patient information and informatics; treatment selection and decision-making tools; and interventions and therapies to improve quality of life for patients, survivors, and their families. Underlying all of these efforts should be culturally competent, multigenerational approaches to communicating effectively with diverse patients and family members in multiple clinical and community settings. [J Natl Cancer Inst Monogr 2001;30:125–9]

Over the past decade, surveys have shown that most insured women are receiving recommended regular screening mammograms and clinical examinations in increasing proportions (1). With current compliance rates now approaching 80% in many groups, a resulting national stage shift to earlier breast cancer diagnosis has been observed (2). Building on this positive public health trend, recent advances in the variety and effectiveness of adjuvant treatment options for breast cancer are producing more favorable outcomes for many women with early-stage disease (3). However, considerable effort, application, and discovery lie ahead to extend this progress to women from all backgrounds and in all income levels and groups.

The 1990s: Environmental Influences and Historical Perspective

Prior to the November 2000 National Institutes of Health Consensus Development Conference: Adjuvant Therapy for Breast Cancer, the most recent consensus development conference on breast cancer treatment was in 1990. Key elements of the progress made in breast cancer detection and treatment over this 10-year period are useful in understanding the current patient issues in adjuvant treatment that need attention. The June 1990 consensus development conference “Treatment of Early-Stage Breast Cancer” panel established that breast-conservation treatment was preferable to mastectomy for the majority of early-stage patients in the United States (4). This finding, important to clinicians, was of greatest importance to breast cancer patients and survivors, who were collectively on the brink of a transformation in their attitudes, approaches, and reactions to the disease.

Advocacy

The 1990s were the decade of breast cancer advocacy. The grassroots breast cancer patient advocacy movement gained momentum and visibility in the early 1990s, inspired by the earlier accomplishments and advances brought about by organized and unwavering AIDS activists. With breast cancer no longer considered a taboo subject or “the Big C,” the topic burst on the public scene through extensive media coverage of the National Breast Cancer Coalition’s highly successful “Do The Write Thing” national letter-writing campaign in 1991, which delivered over 600,000 messages to President Bush and members of Congress from every state. The survivors turned activists were articulate and persuasive in demanding expanded breast cancer research efforts, more funding, progressive legislation, and increased involvement of women affected by the disease in key medical and policy decisions (5).

Breast cancer research expenditures at the National Cancer Institute (NCI) rose 64.8% in the period from 1993 to 1998 within a 23.2% overall NCI research budget rise (6,7), largely because of the efforts of this well-organized patient movement. The NCI research budget for other women’s reproductive cancers, prostate cancer, lung cancer, and all other major cancer sites and types reported also rose over this period (7). Activists joined medical professionals in addressing quality issues, reimbursement, and entitlement coverage, including the U.S. Food and Drug Administration (FDA) regulation of mammography facilities through the 1994 implementation of the Mammography Quality Standards Act, the growth of the U.S. Centers for Disease Control and Prevention’s program to screen low-income women for breast and cervical cancer, and extension of Medicare mammography coverage to annual screening.

Awareness

Public- and private-sector education programs in the 1990s featured the personal stories of celebrities, and well-recognized
consumer products companies with household names launched cause-related marketing efforts to increase national awareness of “good breast health.” Public health and media experts joined together in print and broadcast programs to decrease the stigma, myth, and fear frequently associated with the disease. By the late 1990s, the World Wide Web became the newest channel to influence the changing environment of vastly increased breast cancer consumer input. A wide range of information and misinformation—medical and scientific, personal anecdote and commercial perspectives, support and connection, and treatment input—became easy to find and omnipresent, with “24/7” availability and instant delivery at an estimated 17,000 Web sites (Iversion D: personal communication).

**Screening Mammography**

Some notable shifts in U.S. population and breast cancer patient demographics took place in the years following the 1990 consensus development conference on breast cancer treatment. After several unsuccessful medical and government attempts to arrive at a national consensus on breast cancer screening guidelines, inconsistency and disagreement among experts discouraged education efforts, stalled advances in mammography compliance, and confused women. However, by late in the decade, positive outcomes from maturing worldwide randomized trials and European national screening programs became available, and FDA-regulated mammography quality had begun to improve. After a January 1997 consensus development conference on “Breast Cancer Screening for Women Ages 40–49,” most private and public agencies in the United States were able to reach consensus about screening women younger than age 50 years. When revised guidelines were communicated to the public, the majority of leading national breast cancer and cancer agencies and organizations agreed on the need for either annual or “regular” breast cancer screening with mammography starting at age 40 years and regular clinical breast examinations. Screening compliance rates rose in published private and government screening surveys (8, 9). In the 1998 release of 1996 data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) cancer database, a pronounced shift to earlier-stage breast cancer diagnoses, as well as survival improvements, began to be evident (10). According to SEER, over the period from 1983 to 1987, 53% of new invasive female breast cancer cases were diagnosed at “localized” stages, a figure that rose to 62% by 1996 (2, 11). Increased mammography use also resulted in a disproportionate increase in the detection of in situ (preinvasive) breast cancers. While the number of new female invasive cases rose about 5% (from 175,000 to 182,800) over the period from 1990 to 2000, the number of new in situ cases increased by 184% (9, 12).

Broad U.S. population shifts have also contributed their effects. America is “graying,” with a large and growing demographic segment of senior women (13), a group at high breast cancer risk because of age. Women currently in their seventies in the United States face up to a one in 25 chance of being diagnosed with breast cancer over the next 10 years (14), yet they frequently misunderstand risk factors—for example, they assume that their daughters are at greater risk than they are themselves (unpublished data, National Alliance of Breast Cancer Organizations/WeightWatchers Survey, 1999). Senior women, who often retain 1960s and 1970s disease associations (of losing both your breast and your life), continue to comply with mammography screening at one of the lowest rates of any U.S. group (15) despite improved Medicare screening coverage.

Demographics also predict a larger number of breast cancer cases in younger women in the United States, although invasive incidence rates for those women under 60 years of age have remained stable (2). Although the average age at diagnosis for breast cancer in the United States is currently about 64 years of age (2) and 56% of diagnoses occur after age 60 years (8), the aging of the post-World War II generation is swelling the ranks of women in their forties and fifties. As a result, with stable breast cancer incidence rates in these age ranges, over the next several years, the absolute number of women in America diagnosed with invasive breast cancer before age 60 years will be the highest in history, merely reflecting the prevalence of this age group in the U.S. population. Younger women—among those most likely to receive screening mammograms—are relatively well-educated, media-savvy consumers often comfortable with technology. They are increasingly health conscious and are insured and in the workforce more often than their mothers were—age-specific behavior observed in most cultural and population groups (8).

**Disparities and Stage at Diagnosis**

Increased compliance with screening mammography recommendations has resulted in a shift to earlier stage breast cancer diagnosis. However, this shift (and the resulting improvement in survival) has largely been confined to insured and higher income women, for whom mammography is accessible and affordable. Women’s health surveys that have historically shown education and income to be strong determinants of health-seeking behavior reflect consistent trends in breast cancer screening, mammography use, stage at diagnosis, and survival.

In breast cancer, differences in income rather than race predict the greatest disparities in access to screening and treatment, leading to differing health outcomes. The NCI’s SEER cancer database, the largest source for national breast cancer statistics, reports cancer information by race rather than by income, using white and black as principal categories. However, differences between the SEER data for black and white women do reflect the effect of income disparities to some extent. Invasive female breast cancers reported by SEER as localized—an encouraging 62% of all new SEER cases from 1989 through 1996—are early-stage invasive diagnoses (2). Recently published SEER data on breast cancer stage at diagnosis for black and white women includes 1997 stage I diagnoses: the earliest-stage invasive, lymph node-negative cases less than 2 cm in diameter, principally mammographically detected. Illustrating the current disparity in access to care, in 1997, 41% of the SEER breast cancers in white women were diagnosed at stage I, compared with only 28% in black women (2).

**THE 1990S: KEY CLINICAL AND RESEARCH TRENDS**

In considering adjuvant therapy from the patient’s perspective, there have been several important and influential clinical trends since the 1990 consensus development conference. Advances in primary and localized treatments—especially less radical mastectomy and increasing acceptance of breast-conserving treatment—have overcome certain morbidities and have been responsive to quality-of-life concerns. However, important open questions in primary and local breast cancer therapy, such as the usefulness and appropriate application of postmastectomy radia-
tion therapy, still remain unresolved. Research showing the benefit of adjuvant systemic therapy for early-stage disease was widely reported and well publicized, beginning with a “Clinical Alert” (16) from the NCI in the late 1980s. A series of studies and trial results published through the 1990s reported decreased recurrence and improved survival benefits from adjuvant therapy as new combinations and sequences of agents created more choices and asked patients to evaluate probabilities and statistics and to trade-off benefits and side effects. Among the many open issues in this area that are critical for patients are questions of dose density and dose intensity, hormonal versus cytotoxic agents and their combinations, and the interdigitation of local and systemic approaches.

With expanding adjuvant therapy strategies, approaches, and agents, patients and their families require more information, more complex and diverse input, and effective communication from their medical teams to make informed treatment decisions. However, as more women with breast cancer must make more complicated treatment decisions, the advent of managed care has meant that time for individual patient interaction is shrinking in offices and clinics. In addition to more prepared, communicative, and empowered breast cancer patients being diagnosed in the decade of advocacy, a new focus on “patient-centered” (as opposed to “tumor-centered” or “disease-centered”) areas of cancer research has helped medical and oncology professionals to perceive and address this communication challenge. In disciplines formerly overlooked or rejected as “soft science,” researchers began to recognize and assess the longer-term physical impact of adjuvant treatments as well as the emotional, sexual, societal, and psychosocial quality-of-life effects of breast cancer. Influential breast cancer advocates have had dual roles, by internalizing, even under nonstressful conditions, and are pre-

SHORTCOMINGS OF CURRENT APPROACHES TO ADJUVANT THERAPY

Despite its progress and achievements, state-of-the-art adjuvant therapy for breast cancer has multiple shortcomings from the patient's perspective, both on the macro level and for the individual patient. In terms of bigger-picture issues, adjuvant therapy is generally recommended by physicians and selected by patients by correlating a woman’s tumor characteristics (and, to a lesser extent, personal factors such as her age) with historical trial and research outcomes. Although scientifically based and data driven, this method assumes homogeneity among trial populations and makes broad assumptions about the applicability of trial results to very diverse individual women. The long-term outcomes of population-based treatment studies that opened for enrollment more than 15 years ago—especially since they attract fewer than 5% of U.S. breast cancer patients (17)—may not be a good match with the highly heterogeneous women who are breast cancer patients in the United States today.

A second major drawback of current adjuvant therapy is that it is not sufficiently individualized. Only very rudimentary tumor and patient characteristics are currently used as prognostic or predictive factors to forecast risk of recurrence and treatment effectiveness. As a result, this approach overtreats some women who would remain disease free with lower doses or different treatments or none at all, exposing them unnecessarily to morbidity, expense, and side effects. At the same time, it undertreats or incorrectly treats women whose breast cancer recurs, exposing them to a high risk of dying of the disease. Women who can be identified in the undertreated or overtreated groups are evident only in retrospect, through later symptoms.

Among other large-scale problems is that the effectiveness of current therapy is limited: It is still not a cure. We cannot predict the impact of short-term or long-term therapeutic side effects or monitor future response to adjuvant therapy while it is ongoing, so we cannot yet change therapeutic courses if a treatment becomes ineffective. Clinical trials that establish future directions for adjuvant therapy take considerable time from design to completion, are expensive, often produce only incremental results, and offer limited provider and patient incentives for enrollment. Few studies and even fewer data exist on patient choice topics (such as treatment decision making, risk assessment, and quality-of-life effects) that could improve women’s clinical trial experiences and raise enrollment as a result. Both the medically underserved and women in diverse minority populations—an increasing percentage of breast cancer patients—are not well represented in many trials and too often do not receive state-of-the-art treatment.

For the individual patient, adjuvant therapy is a complicated opportunity, offering the promise of benefits as well as substantial drawbacks. Making informed therapy choices requires immersion in medical information and the consideration of difficult decisions made rapidly after diagnosis, and women can feel unprepared and overwhelmed. Therapy selection is often based on quantitative factors and abstractions, such as percentage lower chance of recurrence, relative risk, and gain in percentage likelihood of surviving 5 years, all ranging from certainty to the unknown. These concepts can be difficult to comprehend and internalize, even under nonstressful conditions, and are presented by medical professionals in the absence of widely published research on accepted, effective communication techniques and tools. In addition, experts have observed limited “numeracy” among adult Americans, who have low levels of facility and comfort with percentages and quantitative factors (Iverson D: personal communication).

More easily understandable by patients, but too often incompletely explained or not communicated well enough by health care professionals, are treatment-related side effects like hair and fertility loss, nausea, hot flushes, and effects on cognition and memory, as well as what can be done to avert, reverse, or ameliorate them. Even less is disclosed, and far too little is understood, about the toxic effects of longer term treatment, such as cardiac damage and secondary cancers, and about an individual woman’s safe tolerance level and lifetime capacity for any one powerful chemotherapy drug. As new agents move rapidly to the clinic before their longer term and side effects are well known, “informed consent” becomes a moving target, and approaches not mentioned by the physician cannot be considered by the patient. Too often, women commence adjuvant therapy with inadequate information and preparation for its physical and emotional effects and, frequently, individual responses differ. While in active treatment, over the short term, a patient can experience an emotionally fragile state in which it is difficult to predict and plan; when treatment is complete, patients take on the burden of living with the risk of recurrence. Once breast cancer is diagnosed, there is little emotional relief.
MAKING IT BETTER: FEATURES OF IDEAL ADJUVANT THERAPY

Science is advancing from its current state of knowledge to the certain prevention and cure of breast cancer. In the meantime, if physicians could offer and women could choose from a range of adjuvant therapy options for breast cancer, what would be the ideal characteristics of that therapy? From the patient’s perspective, adjuvant breast cancer treatment options should be clinically well understood, selective, tailored, well communicated, and effective. More about each characteristic is explained below.

Clinically well understood means that the patient can obtain both qualitative and quantitative information about the therapeutic option, available to her from multiple accessible and understandable sources that amplify, complement, and confirm what she needs to know. Sources for input would include her physician and medical institution, the peer-reviewed oncology literature, reliable and familiar information sources that she trusts (such as nonprofit and government organizations and agencies), and other women and patients in support groups or other settings. Both qualitative and quantitative information would be available about treatment risks (e.g., morbidity and mortality, their variability and likelihood) and treatment benefits (e.g., recurrence, survival; side effects; and practical, economic, and quality-of-life aspects). The information would address risks and benefits during active therapy, over the short term, over longer term follow-up, and into survivorship. It would embrace all aspects of the woman’s personal and family life as well as treatment effects on her life partner, close family members, friends, and coworkers.

Selective means that the treatment is most likely to maximize disease response and prevent recurrence with the fewest, or no, adverse side effects. Its choice would be based on her disease specifics, features and characteristics, her personal health and cancer history, her family health history and genetic profile, and the state of her overall health.

Tailored treatment is individualized treatment, chosen while taking into account the patient’s personal priorities, reactions, preferences, and attitudes about risk, side effects, and quality of life. Considerations would include her point of view about symptom trade-offs, reserving future treatment and drug capacity, and her perception about the sequencing of options; her ranking of the importance of side effects, including those that can be modified (and how), and those that cannot; and the meaning to her of various dimensions of quality of life—both in her life at the moment and as she projects her future, both at work and at home. Treatment would consider how and when she most values clinical research and contributing a legacy to future generations, as well as process-oriented aspects of trial participation: consent, randomization, privacy, and monitoring.

Tailored treatment would also take into account the patient’s age, stage of life, and personal priorities, including physical—strength and physical requirements at work and at home, capacity for energy and reserves, fertility and sexual issues, and tolerance for hot flushes, flashes, and night sweats; cognitive—how and when she most values stability/transience of mood, acuity, focus, and memory; emotional—issues about depression, anxiety, and body image, including the effect of partnering status and other support systems; and practical—treatment costs and adequacy of reimbursement, her physical mobility and availability of transportation, obligations of dependents, and requirements for predictability/tolerance for variability.

Well-communicated treatment options are conveyed and discussed using language and decision-making methods that are understandable, meaningful, and successful and that assist and support the individual woman in making informed, confident decisions. Medical providers who are effective communicators can assist the patient in this process by helping her to listen, hear, absorb, and understand the information and choices that are being suggested (see Table 1). Although additional tools and techniques are needed, existing effective approaches should be used to put the patient at ease, to establish informative two-way communication, and to both permit and encourage the woman to compare appropriate alternatives side by side in partnership with her health care team (see Table 2). Well-communicated treatment discussions empower the patient to take an active role in making decisions that will affect the length and quality of her remaining life. In some cases, a recurrence-free future is beyond the promise of current science and, for these cases above all, well-communicated options include each treatment’s limitations.

<table>
<thead>
<tr>
<th>Table 1. Communicating breast cancer adjuvant therapy options: steps in effective patient/provider communication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Help the patient to . . . By these approaches to communication . . .</td>
</tr>
<tr>
<td>Listenable . . .</td>
</tr>
<tr>
<td>Hears . . .</td>
</tr>
<tr>
<td>Absorbs . . .</td>
</tr>
<tr>
<td>Understands . . .</td>
</tr>
<tr>
<td>Compares . . .</td>
</tr>
<tr>
<td>Considers . . .</td>
</tr>
<tr>
<td>Decides . . .</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Communicating breast cancer adjuvant therapy options: recommended approaches that encourage and empower the patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encourage the patient to . . . With this result . . .</td>
</tr>
<tr>
<td>Relates her breast cancer story . . .</td>
</tr>
<tr>
<td>Explains her life . . .</td>
</tr>
<tr>
<td>Reveals her decision-making style . . .</td>
</tr>
<tr>
<td>Expresses fear and anger . . .</td>
</tr>
<tr>
<td>Challenges and questions . . .</td>
</tr>
<tr>
<td>Explains daily needs . . .</td>
</tr>
<tr>
<td>Finds resources and information . . .</td>
</tr>
<tr>
<td>Seeks out survivors . . .</td>
</tr>
<tr>
<td>Feels empowered . . .</td>
</tr>
</tbody>
</table>
and an unwavering commitment to tell the truth as the medical team knows it. For many patients, knowing what to expect, even if it is not the best outcome, can reduce anxiety.

Effective treatment is treatment that works—in the adjuvant setting, treatment that delays or prevents the recurrence of breast cancer. However, to be effective for an individual woman, even therapy with this successful end result must have an acceptable price in its effects on her life. And for patients with higher risk disease where prevention of recurrence may not be a realistic outcome, the definition of effective therapy will vary. Ultimately, the choice is the patient’s, once the medical professional has met the obligation of clearly communicating the most appropriate, tailored, and selective adjuvant treatment options available. In providing effective choices, the professional has the obligation to take direction from the patient, to advise of and explain clinical research options, to update and reassess when new information becomes available, and to consider complementary and alternative therapies. Effective therapy can include pausing to rethink and reconsider and always includes the prompt, private, and sensitive delivery of bad news.

Adjuvant Therapy for Our Daughters

What adjuvant therapy for breast cancer does the future hold? Not so far away, for our daughters or for their daughters, may be universal breast cancer prevention, perhaps as a vaccination. An educated and proactive public could obtain risk profiles early through simple tests when all of the causes of breast cancer are known. Adjuvant therapy may no longer be necessary when better screening and imaging techniques make truly early “early detection” possible, when a breast cancer is still a mere clump of cells. Then, perhaps the errant cells could be reprogrammed or minimally invasive ablation could be possible, similar to how a small skin cancer is treated today—on a woman’s lunch hour. Successful tumor-specific strategies coupled with patient-specific approaches would be independent of today’s seemingly insurmountable time, reimbursement, and access problems. Although these may sound like distant possibilities, the combined power of advocacy, passion, science, and research have brought us far closer than we were just 10 years ago. Progress in adjuvant breast cancer therapy advances us further on the path to the future, to healing the immense pain and loss that breast cancer causes, and to eliminating its current, vast threat to America’s women and their families.

References


Notes

1. Editor’s note: SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

The author is an employee of the National Alliance of Breast Cancer Organizations, which has received unrestricted educational grants from one or more corporations that manufacture products that relate to the National Institutes of Health consensus development conference subject matter.