



Value-Based Oncology BENEFIT DESIGN™

Balancing Cost, Quality, and Access in Chronic Myelogenous Leukemia Treatment

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Target Audience

This activity was developed for pharmacy directors, P&T Committee members, managed care pharmacists, oncology pharmacists, and other key stakeholders who wish to enhance their knowledge concerning the implementation of a value-based benefit design for cancer care.

Learning Objectives

At the completion of this educational activity, participants should be able to:

- Identify the intersection of epidemiologic shifts in the American cancer patient population, new cancer drug costs, and new diagnostic modalities on achieving value in clinical treatment
- Recognize the role of value (cost, quality, access) in the new value-based healthcare system and the incentives for payers and purchasers to meet each of these 3 aspects of value in cancer care
- Understand how the NCCN clinical practice treatment guidelines are aiding all stakeholders in attaining value-based cancer care amidst rising new product costs
- Incorporate value-based care in the treatment of chronic myelogenous leukemia

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Mission Statement

Value-Based Oncology Benefit Design provides payers and others involved in overall healthcare resource allocation with the information they need to make competent formulary and benefit design decisions. The sharp escalation in the cost of cancer care is threatening the financial stability of the healthcare system and has become a major area of strategic focus for payers, purchasers, government, and other stakeholders. New cancer therapies must meet a triad of qualities to find acceptance by payers—cost, quality, access—the value proposition for all healthcare interventions.

Chronic Myelogenous Leukemia Therapies

Chronic myelogenous leukemia (CML) is a cancer of the blood-producing cells of the bone marrow that results in an overgrowth of white blood cells.¹ Also called chronic myeloid, chronic myelocytic, or chronic granulocytic leukemia, CML comprises an estimated 15% of adult leukemia cases.² Occurring primarily in adults and rarely in children, CML is more prevalent in men than women (median age at diagnosis, 66 years).³ Approximately 4830 Americans (2800 males, 2030 females) were diagnosed with this type of cancer in 2008.¹ It is estimated that more than 21,500 people in the United States have CML.⁴ From 1999 to 2005, the overall 5-year relative survival rate for patients with CML was 56.1%.³

Most cases of CML are associated with a mutated chromosome known as the Philadelphia (Ph) chromosome, which generates an abnormal protein that leads to an overproduction of immature, poorly functioning white blood cells.⁵ If CML is suspected, blood and bone marrow samples are tested for the Ph chromosome or the *BCR-ABL* fusion gene.⁴

CML has 3 phases—chronic, accelerated, and blastic (Table). Approximately 90% of patients are in the chronic phase at the time of diagnosis.¹ Some patients progress from the chronic phase directly to the blast phase.⁶ If untreated, the disease can progress from the chronic phase to a fatal blast phase in 3 to 5 years.²

Patients with CML, including those in remission, should have follow-up examinations at regular intervals to check for signs and symptoms of recurrence or for late effects; they should also be encouraged to avoid smoking, eat a balanced diet, maintain a healthy weight, and be screened for other types of cancer.

Recent Advances in CML Therapies

Once a fatal disease without stem-cell transplant, CML now has much better long-term outcomes and is one of the most manageable hematologic malignancies.⁷ CML treatment was revolutionized several years ago by the development of imatinib, a potent and specific inhibitor of the *BCR-ABL* tyrosine kinase.² Before the introduction of imatinib, 5% to 10% of patients with CML died within 2 years of diagnosis, and 10% to 15% died annually thereafter.⁶ Today, the estimated 6-year overall survival for patients treated with imatinib is 88%, and 93% of patients do not progress to the accelerated or the blast phase of the disease in the first 6 years of treatment.^{2,8}

The outlook for patients with CML is promising. Recent findings on genetic mutations and other pathways involved in CML have led to the development of new, even more potent tyrosine kinase inhibitors.² Genetic testing and

other molecular markers have begun to transform the way cancer is being treated with targeted therapies for specific subpopulations.

Recent advances have spawned the discovery and development of promising new cancer therapies that have helped to improve outcomes. New treatments have had a dramatic impact on the survival, quality of life, and productivity of patients with cancer. However, these new agents are also associated with increased costs, and for many products, no generic alternatives are yet available. The use of anticancer drugs increased by 24% in 2008 and is expected to increase by 34% in 2009.^{9,10} Current oral drugs for cancer represent an estimated 20% of a health plan's overall spending in cancer treatments, and their utilization is expected to increase by 25% annually.^{9,11}

Treatment Strategies

There are 6 standard treatment types for patients with CML—tyrosine kinase inhibitor therapy; chemotherapy; biologic therapy; high-dose chemotherapy with stem-cell transplant; donor lymphocyte infusion; and surgery to remove the spleen.

Considerations for treating CML with tyrosine kinase inhibitors include the stage of the disease, the medication's side-effect profile, and the agent's relative effectiveness against *BCR-ABL* gene mutations.²

Imatinib Mesylate

The oral therapy imatinib mesylate is considered standard-of-care first-line therapy for chronic-phase CML.^{2,8} The National Comprehensive Cancer Network (NCCN) clinical practice guidelines recommend primary treatment of chronic-phase CML with imatinib mesylate for patients with the Ph chromosome or with the *BCR-ABL* gene.² Although treatment with interferon immunotherapy has shown a 10% to 15% complete cytogenetic response, with a median survival of more than 10 years, the NCCN guidelines recommend that interferon no longer be considered as initial therapy, because of the excellent long-term results with imatinib.² For the rare patients who are unable to tolerate imatinib, the guidelines recommend therapy with alternate tyrosine kinase inhibitors, interferon, or participation in a clinical trial.²

Findings from the International Randomized Study of Interferon vs ST1571 (IRIS) trial demonstrated the safety, efficacy, and excellent survival benefit for patients with newly diagnosed CML treated with imatinib mesylate.^{12,13} The recommended initial dose of imatinib is 400 mg/day, and higher doses for patients with relapsed disease, provided they can tolerate the higher doses.²

Ongoing studies are being conducted on the dose escalation of imatinib. Initial studies showed the efficacy of high-dose imatinib, which was well tolerated, but also resulted in increased myelosuppression. The NCCN guidelines suggest that additional studies are needed to evaluate the efficacy of higher initial doses, and that treatment response to imatinib therapy be monitored (with cytogenetics and reverse transcription-polymerase chain reaction) at 3, 6, 12, and 18 months.²

Imatinib is generally well tolerated, and most adverse events reported are mild to moderate.¹⁴ The most common side effects reported with this agent include fluid retention, muscle cramps or pain, abdominal pain, vomiting, diarrhea, abdominal bleeding, nausea, fatigue, and rash.¹⁴

Although primary resistance to imatinib is rare, some patients may develop secondary resistance associated with a mutation of the BCR-ABL gene, which can result in disease progression.² If patients with CML become resistant to imatinib, some patients will have intolerable side effects.⁵ The frequency of resistance to imatinib increases in the advancing stages of CML.¹⁵

Second-Generation Tyrosine Kinase Inhibitors

The second-generation tyrosine kinase inhibitors dasatinib and nilotinib were developed to treat patients with imatinib-resistant CML, by acting against the same abnormal protein targeted by imatinib, but in different ways.⁵ Both are oral medications that have been shown to be safe and effective in patients with imatinib-resistant or imatinib-intolerant CML.² In phase 1 trials, patients with imatinib-resistant CML responded well to either dasatinib or nilotinib.⁵

Treatment with dasatinib or nilotinib is recommended for patients who progress to the accelerated-phase CML while using imatinib, or for those with chronic-phase CML who do not respond to imatinib. However, only dasatinib is recommended for patients who progress to the blast-phase CML while using imatinib.²

Several clinical trials are now being conducted on dasatinib and nilotinib to investigate the use of these second-generation agents as first-line treatments for CML, as well as in combination with other treatments, such as chemotherapy; interferon; or cancer vaccines. The role of these drugs in stem-cell transplants is also being investigated.

Dasatinib. Initial findings from a phase 2 study for 186 patients previously treated with imatinib who took dasatinib twice daily showed that in 90% of patients, the abnormal white blood cells characteristic of CML either disappeared or were reduced to very low levels.⁵ In addition, in 52% of patients, the Ph chromosome either disappeared from the bone marrow or was reduced to very low levels, and 92% of patients were still free of disease progression after at least 8 months of follow-up.⁵ The most common side effects reported were low white blood cell count, headache, diarrhea, fatigue, shortness of breath, and skin rash; 6 patients (3%) had pleural effusion.⁵

Table The 3 Phases of Chronic Myelogenous Leukemia	
Phase	Description
Chronic	<5% blasts (immature leukemia cells) in blood/bone marrow ^a Indolent period lasts months to years
Accelerated (myeloproliferative)	>5%–<30% blasts in peripheral blood/bone marrow ^a Marked by new cytogenetic changes as CML cell mutations increase and grow faster Possible treatment failure, worsening anemia, progressive thrombocytopenia
Blastic (blast crisis)	>30% blasts in peripheral blood/bone marrow ^a Develops if CML cells behave like acute leukemia Symptoms include fever, malaise, enlarged spleen, weight loss Tumors may develop in bone, lymph nodes, skin, central nervous system

^aThe percentage of blast cells for each phase varies in the literature. CML indicates chronic myelogenous leukemia.

Sources: American Society of Clinical Oncology. Leukemia—chronic myeloid—CML. Overview. July 9, 2008; Chronic leukemia. In: *Merk Manual (Professional)*. Revised June 2008.

Nilotinib. Results from a phase 2 study of 280 patients previously treated with imatinib who took nilotinib twice daily demonstrated that after at least 6 months of follow-up, almost half of the patients responded to nilotinib treatment.⁵ The Ph chromosome was eliminated from the bone marrow in 31% of the patients and was reduced to low levels in 16%.⁵ The most common side effects reported were mild skin rash, nausea, fatigue, and headaches. Approximately 30% of patients showed moderate to severe drops in white blood cell count or in platelet levels.⁵

Cramps and weight gain, side effects associated with imatinib treatment, were uncommon with nilotinib treatment in this study. In addition, side effects associated with both imatinib and dasatinib—fluid in the lungs and swelling of the legs, ankles, and feet—were rare with nilotinib in this study.⁵

Other Available Treatments

Interferon. The injectable biologic interferon, administered daily, was the primary treatment for chronic-phase CML prior to the availability of imatinib.⁴ Interferon is associated with flulike side effects, and when given on an ongoing basis, it may cause fatigue, loss of energy, and memory changes.⁴ In addition, before imatinib was available, allogeneic stem-cell transplants were offered to appropriate candidates, and in some cases these transplants resulted in a

cure for CML.⁴ However, because the procedure is associated with a 10% to 20% risk of death, it is usually now reserved for patients who do not respond to, or become resistant to, imatinib.⁴

Donor lymphocyte infusion. Another treatment is donor lymphocyte infusion, which may be used after a stem-cell transplant. In this treatment, lymphocytes are removed from the stem-cell transplant donor blood, frozen for storage, and then thawed and given to the patient through 1 or more infusions. The lymphocytes respond to the patient's cancer cells as invaders and attack them.

Oral chemotherapy. Hydroxyurea, an oral chemotherapy drug, is another option sometimes given to patients initially to reduce the white blood cell count until a definite CML diagnosis is made.¹⁵

Emerging Therapies and New Targets

Once researchers identified the main cause of CML (BCR-ABL gene and its protein), they began developing new drugs to target these sources.¹⁶ Bosutinib, an investigational kinase inhibitor, is being compared in clinical studies with imatinib. Early studies show that bosutinib is effective in patients in all phases of CML, and that it may be less toxic than other currently available tyrosine kinase inhibitors.¹⁶

Another investigational agent is INNO-406, a dual BCR-ABL and Lyn-kinase inhibitor. Early clinical data show that this drug has worked in some patients who do not respond to currently available tyrosine kinase inhibitors.¹⁶

MK-0457 (VX-680), an aurora kinase inhibitor, is yet another investigational drug that has been shown to work against cells with a *T3151* gene mutation, which causes cells to become resistant to current targeted therapies.¹⁶

The addition of a drug that inhibits a cell process called autophagy may enhance the therapeutic effects of tyrosine kinase inhibitors in the treatment of CML, according to results of a new study.¹⁵ Bruno Calabretta, MD, PhD, one of the study's investigators, says that combining chloroquine (an autophagy inhibitor) with imatinib appears to potentiate imatinib-induced cell death; he also notes that additional effects of the drug have not been studied in detail.¹⁷

Researchers have recently identified a mutant gene that is linked to aggressive leukemia.¹⁸ A genetic change in the Ph chromosome (*BCR-ABL1*) alters the gene *IKZF1*, which produces the protein Ikaros. Ikaros plays a key role in regulating the normal development of lymphocytes. In their effort to identify genetic abnormalities in acute lymphoblastic leukemia, researchers analyzed 23 cases of CML, which also involves *BCR-ABL1*. The researchers observed Ikaros deletions at the progression of CML to lymphoid blast crisis, indicating that Ikaros mutations may help determine the behavior of *BCR-ABL1* leukemia.¹⁸ These and other recent findings may help predict responses to the treatment of CML or minimize resistance to treatment.

Clinical trials are being conducted on LBH589, a novel

deacetylase inhibitor that induces cell apoptosis at nanomolar levels.^{19,20} Preclinical studies showed that when LBH589 is combined with imatinib, it is effective at eliminating CML cells, including leukemia stem cells. It is hoped that this combination therapy will eliminate the threat of relapse for CML patients taking imatinib.^{19,20}

Recent advances in tumor antigen discovery have been incorporated into the design of new clinical studies on CML, and recent data have provided useful information on the interaction of tyrosine kinase inhibitors with the immune system.²¹

A number of vaccines are also being investigated for use against CML. Ultimately, researchers hope that recent findings and advances in immunotherapy will help them develop a cure for this disease. ■

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CML: Balancing Cost, Quality, and Access

The US healthcare landscape is evolving, and major policy reform is anticipated over the coming months and years. There is a growing movement toward universal access to healthcare, preventive medicine and wellness, improved productivity in schools and the workforce, and improved healthcare delivery outcomes in terms of quality and cost. Collaboration and integration among key stakeholders has become essential. And with many baby boomers entering the elderly population, chronic diseases will become a major component of healthcare resource utilization.

These shifts demand new paradigms that bring value and new strategies for all healthcare stakeholders in their efforts to improve system-wide outcomes while navigating through inherent complexities. Although changes and challenges abound, the environment is ripe with opportunities for a new direction. There is a push to rethink former approaches in terms of aligning care services into an integrated system, plan for the continuum of patient care, and formulate practical approaches to benefit design within the current dynamics of healthcare resource allocation, particularly for patients with cancer and other chronic diseases.

Today, products must meet a triad of entities—cost, quality, and access—to achieve value for all stakeholders, including payers, employers, patients, providers, and manufacturers. Payers will no longer reward a novel therapy based only on its innovation or allow a provider to prescribe a treatment based merely on theoretical applications.¹ The rise in cancer drug costs over the past decade has caused payers and purchasers to apply cost-containment measures for new drugs, whereas in the past, quality reigned alone in the fight against cancer.¹ New oncology therapies must offer more than innovation to survive in an increasingly restricted, fiercely competitive, and cost-sensitive environment.¹

Payers and purchasers must create benefit design models that balance cost, quality, and access to care. Even widely successful targeted therapies will require a convincing cost/quality value proposition. Evidence-based clinical practice guidelines for cancer therapy and supportive care can provide a strong framework for cost-effective utilization. The viability of our healthcare system hinges on the ability to treat our increasing aging population through value-driven, evidence-based, patient-centric benefit designs.

Chronic myelogenous leukemia (CML) most often affects individuals in their 60s, meaning that a large number of patients with CML are likely to be Medicare beneficiaries. According to the National Cancer Institute (NCI), Medicare accounted for 45% of spending on all cancer treatments in 2004.² As a result of the high cost of many oral medications for cancer, some patients will enter the no-coverage gap (or “doughnut hole”) of Medicare Part D after a single prescrip-

tion, and may be in the same situation year after year, because the cost cycle repeats at the beginning of each calendar year.² Addressing this coverage gap is one of a number of heated topics being discussed these days in Washington, but the cost of doing away with the coverage gap is staggering.

According to the NCI, an estimated \$2.6 billion is spent on the treatment of leukemia in the United States.³ Although the NCI investment in leukemia research increased between fiscal years 2003 and 2006, it actually decreased to \$205.5 million in 2007.³

Cost of CML Therapy

According to the *2007 Drug Trend Report*, the average cost per prescription for a drug used to treat cancer was \$1816 in 2007, although imatinib mesylate—the standard first-line therapy for chronic-phase CML—cost as much as \$3109 per prescription.^{4,5} However, findings from 2 recent studies show that the high price of imatinib is offset by the expected increase in survival rates in patients who are treated with this medication.^{6,7}

Unlike the second-generation tyrosine kinase inhibitors dasatinib and nilotinib, imatinib has been shown to increase survival.⁸ New evidence shows that the 6-year survival rate with imatinib is 88%.⁹ Using a novel method of estimating the long-term survival benefit of new medical therapies for CML, one analysis concluded that patients with CML who take imatinib as a first-line therapy would survive for an estimated 6 years longer than those treated with interferon-alpha therapy.⁷ And according to projected treatment costs and survival estimates, researchers calculated the incremental cost of imatinib at \$43,100 per life-year saved in 2004, when the accepted cost threshold for medical therapies was \$50,000.⁶

Another study examined the association between medical costs and imatinib adherence in patients with CML (n = 404), showing that not adhering to treatment with imatinib may lead to suboptimal clinical outcomes.¹⁰

The authors concluded that better imatinib adherence was associated with significantly lower costs for CML patients, particularly in inpatient costs, and that further analysis would be needed to confirm whether lower adherence resulted in more hospitalizations.¹⁰

The economic cost of mortality from cancer is high in the United States, both in terms of lost work productivity and the value of 1 year of life, according to the findings of 2 recent studies.^{11,12} In 2000, cancer deaths cost the United States \$115.8 billion in lost productivity, and that cost is expected to jump to \$147.6 billion in 2020, based on the size and age of the population.¹¹ A 1% annual reduction in mortality, using current trends from leukemia, lung, breast, colorectal, pancreatic, and brain cancer, could reduce this esti-

mate by \$814 million annually.^{11,12} When the study authors included the value of caregiving and household duties lost, in addition to regular wage earning jobs, the cost of cancer mortality more than doubled, to \$232.4 billion in 2000, and is estimated at \$308 billion for 2020.¹¹

The authors concluded that these cancer mortality costs are a key component of the burden of disease, and that this information is important to decision makers for assessing the costs of interventions and determining resource allocation.

Access to Quality Care

Findings from a Kaiser Family Foundation study show that the number of working-age adults who reported having at least 1 of 7 major chronic conditions grew by 25% from 1997 to 2006, to a total of nearly 58 million people in 2006.¹³

More privately insured and uninsured patients with chronic conditions reported an unmet need for care because of costs, and those with Medicaid coverage experienced no change.¹¹ However, the uninsured were more than 4 times as likely as the privately insured to experience an unmet need for care (35% compared with 8%, respectively).¹³ In the privately insured group, those reporting access-to-care problems nearly doubled, increasing from 5% in 1997 to 9.5% by 2006.¹³

The study investigators concluded that access to care for those with chronic conditions is eroding, even for individuals with private insurance. They also observed that this trend is particularly concerning, and controlling healthcare system costs demand effective and efficient care for people with chronic conditions, because they are the ones who use the majority of healthcare services in the United States.¹³

Increasingly, many patients who undergo treatment for cancer maintain their jobs and continue to produce at work. Chronic health conditions can place a significant financial burden on individuals, employers, and health plans.¹⁴ Those involved in benefit design need to find solutions that are cost-effective for both employers and employees, so that employees could access necessary services and remain productive. Shifting costs to patients may backfire by leading to nonadherence and increased costs elsewhere.¹⁴

Access to care may be further jeopardized until appropriate measures are taken to make healthcare more affordable to patients. Both private and public insurance plans in the United States often require patients to absorb the burden of costs for cancer therapies.² Oral chemotherapy is generally covered under the pharmacy benefit, which tends to require higher copayments, whereas intravenous infusions are traditionally covered under the medical benefit, which tends to be more generous in its coverage. Spending on oral chemotherapeutic agents more than doubled between 2002 and 2006, from 0.3% to 0.7%.²

Higher drug costs mean that patients reach the coverage gap earlier today than ever before. Nearly 70% of stand-alone prescription drug plans offer no gap coverage, and 13% offer full generic gap coverage.¹⁵

Comparative Effectiveness Research

The American Recovery and Reinvestment Act allocates \$10 billion to the NIH, of which \$1.2 billion is designated for the NCI.¹⁶ This funding will be available through September 2010.¹⁶ The influx of funding for cancer research may have an important impact on scientific advances in the coming years.

The recent push for comparative effectiveness data has had a significant influence on product development and post-launch surveillance, and some manufacturers now routinely select a current market leader as a comparator when designing randomized controlled clinical trials.¹⁷ Other manufacturers are reluctant to conduct costly head-to-head comparative effectiveness studies.¹⁸ Major hospitals/teaching institutions are also getting more involved with comparative effectiveness research (CER), conducting meta-analyses of clinical trial literature in specific product areas to determine what products will be used.

Payers will be looking at CER results to determine what the tradeoffs are in the very expensive products (drugs, biologics, devices) for specific diseases.¹⁸ Evaluating the clinical and economic performance of drug and device therapies is a wave of the present and future and will likely continue to influence healthcare innovation. ■

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Cost-to-Benefit Comparisons in Pharmacy Decisions

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From the perspective of a health plan pharmacy department, 2 of the most useful pieces of information are (1) comparative or head-to-head studies, and (2) pharmacoeconomic and outcomes data.

The comparative data allow a plan to clearly differentiate between drugs in a single class, and/or between a new therapy and the current standard of care. Until such evidence is available, we are limited to studies of individual drugs, which makes benefit decisions an approximation of which drug will be best in a given situation.

The pharmacoeconomic and outcomes data, which go hand-in-hand, allow the payer to clearly compare the cost-to-benefit ratio of each drug. It is very useful to be able to see what the actual cost of therapy will be. That is, what will be the number needed to treat to benefit 1 patient, and what will be the outcomes if a particular drug is used versus another.

Such data also demonstrate whether the patient's condition is likely to improve, that is, if a drug will bring a patient into remission or just temporarily halt the disease progression. This is always an important factor when choosing one therapy over another, but the cost-to-benefit comparison is especially critical in the current economic environment. Just as members/patients expect good value for their premium costs, so do health plans expect that the best drug will actually improve patient outcomes and decrease the need for adjuvant therapies and the overall cost of treatment.

One of the greatest aids in choosing a cost-effective therapy for chronic myelogenous leukemia (CML) has been the development in recent years of clinical treatment guidelines. Major organizations, such as the National Comprehensive Cancer Network, the American Society of Clinical Oncology, and the American Society of Hematology, provide evidence-based clinical guidelines that list best thera-

pies for specific clinical situations but also take cost considerations into account. These guidelines recommend different drug options so that providers have a choice of therapies for any given patient.

The cost of dasatinib is significantly greater than that of nilotinib, but if a patient has not responded to or is intolerant of imatinib and has progressed to the blast phase of CML, dasatinib is the best alternative available.

After the provider chooses a therapy, the health plan may ask that provider if a less costly alternative may be as effective. For example, a provider may initiate therapy for a patient with CML (at any stage of the disease) with the first-line oral treatment, imatinib. However, if that patient cannot tolerate the drug, the provider may change the prescription to one of the second-line oral therapies—dasatinib or nilotinib. Based on drug costs alone, the second-line choice may be nilotinib. However, nilotinib is not effective in the blast phase of CML, which may suggest dasatinib as the best option. The cost of dasatinib is significantly greater than that of nilotinib, but if a patient has not responded to or is intolerant of imatinib and has progressed to the blast phase of CML, dasatinib is the best alternative available, given that a tyrosine kinase inhibitor is the treatment of choice for this type of cancer.

There is, however, a downside to these therapies: unlike imatinib, neither of the second-line agents shows an increased survival rate. Nonetheless, evidence-based guidelines indicate that the tyrosine kinase inhibitors are currently our best weapons against CML. If we could only make them more affordable, we would have the best of both worlds. ■

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Oral Therapy for CML and the Nurse's Changing Role

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Chronic myelogenous leukemia (CML) was once a fatal disease, with a limited life expectancy. Not so many years ago, oncology nurses injected patients with interferon-alpha, and intolerable side effects often necessitated discontinuation of interferon treatment. In the past, nurses prepared younger patients with CML for allogeneic stem-cell transplantation, and on occasion were witness to transplant-related mortality. But the identification of the BCR-ABL fusion gene as a drug therapy target prompted the search for an inhibitor and led to the development of imatinib—now the standard therapy for CML.¹

From a nursing perspective, imatinib is an easily administered treatment, since it is an oral agent and is usually self-administered. Because it is well-tolerated, with manageable side effects, patients generally adhere to treatment and can expect promising long-term outcomes. From 1990-1992 to 2002-2004, the overall 10-year relative survival of patients with CML increased from 16% to 72% for younger patients (ages 15-44), and from 8% to 34% for older patients (ages 55-64).² Patients now are able to be optimistic and plan for the future; further advances in CML treatment may one day lead to a cure for this disease.

Now that the treatment of CML has shifted from nurse-administered parenteral therapies to oral therapy, health-care facility fees and nursing costs are reduced. The nurse's role is now focused on teaching patients about CML and its treatment rather than on administering treatment. Patient monitoring has changed as well. Treatment side effects are fewer and less severe than in the past, and patient follow-up now involves periodic clinical, biochemical, hematologic, and cytogenetic monitoring. Most important, patients spend less time receiving treatment in healthcare facilities and have more time to engage in work and leisure activities. Extended life expectancy allows patients with CML to be productive members of society for longer periods of time.

From the patient's perspective, effective CML treatment is desired—at any cost. Even when the costs are high, patients will argue that such cost is justified if they can live longer. Today patients are also sensitized to quality-of-life (QOL) issues. They generally do not want to live longer if their QOL will be low or if they will have to endure pain and

suffering to live longer. Unlike many types of cancer in which treatment response is often suboptimal and life expectancy is reduced, CML is among the few cancer types in which optimal (ie, complete hematologic, cytogenetic, and major molecular) responses and longevity are likely outcomes.

Direct and indirect costs of healthcare are increasingly affecting patients, and the number of those concerned about their ability to access and pay for quality healthcare is growing. Although patients generally are not as concerned with treatment cost-effectiveness as they are with clinical effectiveness, they do play a large role in paying for CML treatment. Direct costs for insured patients include health insurance payments, deductibles, copayments, and noncovered medical expenses. Uninsured and underinsured patients face high direct care costs.

Patients also may be affected by indirect costs, such as lost wages, transportation costs, and payments for household services patients are not able to provide (eg, house-keeping, child care). Intangible costs include the unknown costs and effects (eg, physical, psychological) of delayed CML diagnosis and treatment, because of lack of access to the healthcare system.

Nurses sometimes are the first members of the healthcare team to learn of patients' financial concerns or situations (eg, loss of a job, loss of health insurance). Although nurses work hard to identify community and governmental resources for patients, it is not always possible to ensure continuity of care. Many healthcare parameters are measurable (eg, medical costs) or relatively measurable (eg, quality), but measuring the effect of access to care, or lack thereof, is elusive. In the case of CML treatment, which is now clinically viable and cost-effective, lack of access to treatment may mean that someone with a treatable disease may encounter delays in receiving, or perhaps not receiving, optimal treatment. Healthcare legislation that ensures access to care, continued CML research, and further refinement of CML evidence-based treatment guidelines are needed to provide a cure for all patients. ■

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Cancer Guidelines and Payer Coverage Decisions

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The National Comprehensive Cancer Network (NCCN) clinical practice guidelines, and their acceptance by the Centers for Medicare & Medicaid Services and by major managed care payers for coverage determination in oncologic therapy, are giant steps forward for medicine. Yet the NCCN guidelines extend far beyond the confines of this discipline as a decisive addition to managed care. Notwithstanding its characterization as simultaneously merging cost, quality, and access issues, the guidelines also exemplify the near-perfect combination of these same 3 tenets inherent in managed care and hence herald a new paradigm.

The ever-expanding scientific advancements in medicine have been associated with burgeoning ethical and legal questions. In fact, the march of medical capability has always outpaced our ability to effectively create and promulgate rules and guidelines in step with their utilization, leaving many unanswered questions about the application of justifiable restrictions in medicine. It has also failed to adequately provide answers to questions we sometimes could not even articulate. Nevertheless, managed care has always endeavored to cover the best care that technology and medical innovation could provide.

Since the inception and continued growth of managed care, we have been just ahead of this specter, pursuing every review and decision rigorously, and depending on the latest information available. Even more challenging has been the inner dilemma for those of us who are always in the occasionally unenviable position of having to approve a policy or a decision. In the background of our charge of calling into question a medical procedure, a drug, a treatment option, or an inpatient length of stay, we have always sought to make the right choices based on well-researched and vetted policies and guidelines. Yet, within ourselves we have sought comfort in the integrity of our decisions when

gaps existed in these evolving blueprints for cost-efficient quality care.

In the background of our charge of calling into question a medical procedure, a drug, a treatment option, or an inpatient length of stay, we have always sought to make the right choices based on well-researched and vetted policies and guidelines.

These exercises in pursuit of accuracy and completeness in guidelines on the part of the payer are not only ceaseless, they are also continuously influenced by the flood of new information pouring into the literature, into clinical practices, and ultimately into the committees making the decisions. The advent and acceptance of the concept of evidence-based medicine have markedly added stability to a conceptual framework for making these policies. But in certain disciplines, still lacking was a consciousness on appropriate application of this knowledge, especially in areas where medical advances are not applicable to all potential recipients, such as in oncology. Yet such “guidelines” were still internally derived and promulgated, and challenged when the decision was deemed unacceptable.

With the advent of the NCCN practice guidelines, however, we now have an external validation that adds an element of self-awareness on the limitations as well as the benefits of the advances in science within the discipline. More important, the development and promulgation of the guidelines show sensitivity to the integrity of patients’ hopes, as reflected in their struggles with their illness, thereby ensuring the quality of healthcare delivery and the decisions that surround them. Wrapped within this enigma is the solution for the elusiveness of cost-efficiency: the 3 elements (cost, quality, and access) have emerged, and the most appropriate decisions are assured in the guidelines’ implementation. ■

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