Evolving Strategies for the Management of Multiple Myeloma: A Managed Care Perspective

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The content of this supplement is based on presentations and discussions at the roundtable meeting entitled "Current Landscape of Multiple Myeloma: Topics for Managed Care" held on Saturday, October 5, 2013, at the Grand Hyatt DFW, located at the Dallas/Fort Worth International Airport in Dallas, Texas. The roundtable meeting was sponsored by Onyx Pharmaceuticals, Inc (South San Francisco, CA), an Amgen subsidiary. The multidisciplinary roundtable panel included clinical experts (oncologists and oncology nurses), medical and pharmacy directors from health plans, specialty/oncology pharmacists, representatives from healthcare policy and patient advocacy organizations, and representatives from Onyx Pharmaceuticals, Inc.

The goal of the meeting was to discuss the perspectives of the faculty members on several topics related to the management of multiple myeloma (MM), including advances in treatment, areas of unmet need, future directions for oncology management, and the potential impact of newer payment and practice models. These topics were discussed in the context of the payer audience.

PART I

MM: A Disease Overview

MM is an incurable malignant disorder characterized by the clonal proliferation of aberrant plasma cells in the bone marrow.[1] MM accounts for approximately 10% of all blood cancers in the United States, affecting 0.4 to 5 individuals per 100,000 each year worldwide.[2,3] A spectrum of blood disorders such as monoclonal gammopathy of undetermined significance (MGUS, the presence of abnormal antibodies in the plasma or urine) and smoldering MM[1] often precede the development of MM, and there are a variety of pathways by which a normal plasma cell can become malignant. At first, MM is confined to the bone marrow, but over time the tumor can acquire the ability to grow

Abstract

Current challenges in the management of multiple myeloma (MM) include the changing treatment landscape and the need for better care coordination and improved communication. A roundtable meeting involving key stakeholders (physicians, nurses, pharmacists, managed care professionals, pharmaceutical industry professionals, and patient care advocates) was held to discuss challenges in the management of MM and evolving strategies to address these challenges and improve quality of care for patients with MM. Interventions discussed included the use of a treatment pathway to standardize treatment, decrease costs, and possibly increase efficacy by encouraging adherence to treatment guidelines whenever possible, and the use of an oncology medical home (OMH) to facilitate communication among treatment providers. Challenges to the successful implementation of treatment pathways include the rapid introduction of new therapies and the need to balance efficacy and value. It was stressed that treatment pathways must not prioritize profits over the health and welfare of the patient. Considerations related to the implementation of the OMH include the identification of appropriate measures to evaluate quality, value, and outcomes, and the provider implementation costs related to the OMH model.

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and affect other locations such as the blood, pleural fluid, lymph nodes, organs, and skin, producing a variety of signs and symptoms including anemia, pathologic bone fractures and pain, renal failure, and hypercalcemia.[1,4] Of note, MM is a heterogeneous disorder with highly variable outcomes; whereas some patients with MM may live for only several months, others survive for a decade or more. Similarly, the disease course varies from indolent to aggressive based on a number of genetic factors. Following treatment, patients may experience eventual regrowth of residual tumor, osteolysis, anemia, and immune dysfunction and suppression.[5-8]

The Epidemiology and Pathophysiology of MM

In the United States, it is estimated that in 2013, approximately 78,000 patients were living with MM.[9] In addition, approximately 20,000 people are diagnosed with MM each year in the United States.[9,10] Compared with patients who received a diagnosis of myeloma between January 1971 and December 1996, those who received a diagnosis between January 1997 and December 2006 had a significant improvement (50%) in overall survival (44.8 months vs 29.9 months; $P < .001$).[5] Despite this improvement, late-line patients (International Staging System Stage II or III disease with more than 1 adverse lesion) have a median overall survival of less than 2 years.[5,11]

Importance of MM Compared With Other Cancers

Managed care participants rated breast, colon, rectal, prostate, and lung cancer as the cancers of highest importance to their organizations relative to other cancer types.

The estimated number of deaths attributable to MM in the United States was nearly 11,000 in 2013, and during the years 2003 to 2009, the overall 5-year survival rate was 43.2%.[9,10] At diagnosis, 5% of patients have localized tumors (plasmacytomas) and 95% have systemic disease with generalized bone marrow involvement. Survival is influenced by the stage of myeloma—the 5-year survival in those with localized lesions (67.6%) is substantially higher than that of patients with generalized and more advanced disease (41.9%). Compared with other tumor types, MM is relatively rare, representing only 1.3% of all new cancers in the United States and ranking as the 15th-most common type of cancer. The lifetime risk of MM, defined as the probability of developing or dying from myeloma over the course of an individual's lifespan, has been estimated at 0.7%.[9]

Less than 4% of patients with MM are younger than 45 years, and the median age at diagnosis is 69 years. Most patients are diagnosed between the ages of 55 and 84 years. The incidence of MM is twice as high in African Americans as it is in whites, and it is also more common in men than women. The percentage of new cases is 7.5% in all males, 7.1% in white males, and 14.4% in black males. In contrast, MM is diagnosed in 4.8% of all females, 4.2% of white females, and 10.2% of black females. The median age at death is 75 years, and mortality rates generally increase as age increases.[9] As suggested by the incidence rates, the strongest risk factor for developing MM is advanced age. Other risk factors for the development of MM may include environmental or occupational exposure to herbicides, insecticides, petroleum products, heavy metals, plastics, and various dust particles, including asbestos.[12]

The disease course may follow a variety of pathways.[1] Overall, there is a 1% annual risk of developing MM in a patient with MGUS.[13] The risk of progression from smoldering to symptomatic MM has been reported to be 10% annually during the first 5 years of disease, followed by 3% annually during the following 5 years, and 1% annually for the next 10 years.[14] Patients with MGUS and smoldering MM are asymptomatic with no end-organ damage; in contrast, active MM is typically associated with a number of symptoms that include end-organ damage.[1,3]

Two important underlying characteristics of MM include uncontrolled malignant plasma cell proliferation and immune dysfunction marked by an increased rate of infection and decreased immune surveillance. As plasma cells proliferate, malignant clones do not respond to normal regulatory signals. The relationship between the myeloma plasma cells and the bone marrow microenvironment plays an important role in MM initiation and disease progression through the promotion of tumor cell survival, drug resistance, angiogenesis, and disordered bone metabolism. In patients with MM, levels of several immunologically active compounds are increased, including transforming growth-factor beta (TGF-ß), interleukin (IL)-10, IL-6, vascular endothelial growth factor (VEGF), cyclooxygenase-2 and related prostanoids, and matrix metalloproteinases.[1,15]

Symptoms, Diagnosis, and Testing

The clinical manifestations in patients with MM are due to the presence of the monoclonal protein (M-protein, an abnormal type of antibody) spike, immunodeficiency, and infiltration of abnormal plasma cells in bone marrow.[4]

Table 1. Multiple Myeloma: Clinical Presentation[16,17,20-22]

Signs and Symptoms	Lab Parameters	Radiographic Parameters	Bone Marrow
• Bone pain • Fatigue • Weight loss • Paresthesias • Recurrent infection • Renal failure • Spinal cord compression • Back pain	• Elevated paraproteins-M peak • Low hemoglobin • Hypercalcemia • Low albumin • High β_2 microglobulin • High serum creatinine • High C-reactive protein	• Lytic lesions • Osteoporosis • Fractures	• Increased plasma cells

Table 2. Initial Diagnostic Evaluation[20,24]

Serum	Urine	Bone Marrow Aspirate	Radiography
• CBC with differential and platelet count • BUN/creatinine, electrolytes • LDH • Calcium, albumin • Serum free light chain assay • Quantitative immunoglobulins • β_2 microglobulin • Serum protein electrophoresis • Serum immunofixation electrophoresis	• 24-hour urine total protein • Urine protein electrophoresis • Urine immunofixation electrophoresis	• Morphology • Histology • Cytogenetic analysis • Fluorescence in situ hybridization • Immunohistochemistry +/- flow cytometry	• Skeletal survey

BUN indicates blood urea nitrogen; CBC, complete blood count; LDH, lactate dehydrogenase.
Adapted from NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Multiple Myeloma. Version 2.2014.

Patients may present with a spectrum of symptoms, including pain (due to the destruction of bone), fatigue (due to anemia), and/or peripheral neuropathy (due to the neurotoxicity of immunoglobulins). Of all patients presenting with MM, bone pain is found in 58%, fatigue is identified in 32%, a pathologic fracture is observed in 26% to 34%, and weight loss is noted in 24%.[16-18]

Patients over the age of 50 years should be evaluated for MM if they have had persistent back pain that has continued for over 1 month and 1 or more additional symptoms are noted, including pain that worsens in the supine position, worsens at night or causes the patient to awaken from sleep, is distributed in a band-like formation around the body, or is not relieved by conventional treatments. Additional warnings include the presence of constitutional symptoms and progressive neurological deficits in the lower extremities.[19] The clinical presentation including signs and symptoms and laboratory, radiographic, and bone marrow parameters of patients with MM is detailed in Table 1.[16,17,20-22]

Altogether, the criteria for diagnosis of MM require the presence of 3 factors: the identification of a paraprotein or M protein either in the serum or the urine, the presence of 10% or greater monoclonal plasma cells in the bone marrow, and evidence of end-organ damage.[23] End-organ damage that is associated with MM can be assessed using the CRAB mnemonic to evaluate the tetrad of signs (Calcium elevation, Renal failure, Anemia, and Bone disease).[4] MM can be classified as being asymptomatic (MGUS, smoldering myeloma) or symptomatic/active according to the diagnostic criteria.[23]

The initial diagnosis is based on laboratory results, including blood chemistries and protein electrophoresis (to identify the M-protein spike, characterized through immunofixation) (Table 2).[20,24] The recommended initial workup should also include a history and physical examination as well as the following baseline blood chemistries and laboratory studies to differentiate symptomatic and asymptomatic MM: a complete blood count with differential and platelet counts; blood urea nitrogen (BUN); serum creatinine; serum electrolytes; serum calcium; albumin; lactate dehydrogenase (LDH); and ß$_2$ microglobulin. Decreased kidney function will be reflected by increased BUN and creatinine, and LDH levels help assess tumor cell burden. Tumor burden is reflected by the level of ß$_2$ microglobulin, which is now considered a standard for measuring tumor burden. To determine MM subtype, a number of karyotypic abnormalities can be analyzed using fluorescent in situ hybridization, which is highly sensitive in detecting structural abnormalities of chromosomes. Bone marrow aspiration and biopsy is used to detect and assess bone marrow plasma cell involvement, and a radiographic skeletal survey (RSS) may be used to help evaluate lytic bone lesions.[24]

Evaluation of the M-protein component is important because 97% of patients with MM exhibit M-protein spikes in either the blood or urine.[17] Assessing changes in levels and proportions of various proteins, particularly the M-protein, is necessary to help track the progression of myeloma disease and response to treatment. Urine and serum M-protein testing includes evaluation of 24-hour urine for total protein; urine protein electrophoresis; and urine immunofixation electrophoresis. In addition, serum analysis is used to quantify different types of antibodies (IgG, IgA, and IgM); serum protein electrophoresis (SPEP) and serum immunofixation electrophoresis (SIFE) are used to determine the presence of abnormal antibodies such as the M-protein.[24] Of note, the serum free plasma light chains (FLC) test was introduced in 2001.[25] This is the most sensitive method for detecting the presence of light chains and for following patient response to treatment.[26] Together with the SPEP and SIFE, the FLC yields a high sensitivity for screening of patients with MM and related disorders. In patients with no detectable M component, an abnormal serum FLC ratio can be used to satisfy the criterion for M-protein spike.[27]

Other tests may be useful in certain circumstances, including magnetic resonance imaging (MRI), positron emission tomography (PET) scans, computed tomography (CT) scans, and PET/CT augmented with fluorodeoxyglucose (FDG) to detect metabolically active sites on bone tissue. Imaging is a clinical aid in determining if the patient has progressed from smoldering MM to active MM. National Comprehensive Cancer Network (NCCN) guidelines rate MRI and PET/CT as being more sensitive in detecting bone abnormalities than RSS.[24] Like CT, PET, and combination PET/CT, RSS can detect bone demineralization. MRI findings have been shown to correlate with plasma cell infiltration into bone marrow.[28]

Disease Progression, Survival, and Prognostic Indicators

At this time, MM is staged using the International Staging System, which is used to stage the disease according to levels of serum $ß_2$ microglobulin and serum albumin.[7,24] Stage I is defined as having a serum $ß_2$-microglobulin level less than 3.5 mg/L and a serum albumin of 3.5 g/dL or greater, stage III patients have a serum $ß_2$-microglobulin level of 5.5 mg/L or greater, and stage II patients are defined as those who do not fit the criteria for stage I or stage III. Within stage II, there are 2 categories that include a $ß_2$-microglobulin level less than 3.5 mg/L with a serum albumin less than 3.5 g/dL, or a $ß_2$-microglobulin level between 3.5 mg/L and 5.5 mg/L irrespective of the serum albumin level. Using the ISS system of staging, the median survival has been reported as being 29 months for stage III disease, 44 for months for stage II, and 62 months for patients with stage I MM.[7]

A number of prognostic indicators can be used to determine prognosis in patients with MM; these factors include $ß_2$ microglobulin level, albumin level, LDH level, free light chain ratio, and the presence of certain genes and specific chromosomal abnormalities.[12] The Stratification for Myeloma And Risk-adapted Therapy (mSMART) guidelines rate del 17p, t(14;16), and t(14;20) as high-risk abnormalities; t(4;14), cytogenetic del 13, and hypodiploidy as intermediate-risk abnormalities; and normal cytogenetics and t(6;14) and t(11;14) as standard-risk abnormalities.[29]

The Evolution of MM Treatment

The treatment of myeloma has evolved greatly over time. Rhubarb was used as a treatment in the 1800s; mephalan, corticosteroids, and cyclophosphamide were introduced in the 1960s; and in the 1980s, high-dose therapy and stem cell transplant were first used. Allogenic stem cell transplants are currently performed much less frequently in patients with MM; most stem cell transplants performed are autologous.[30] Novel agents include the proteasome inhibitors (ie, bortezomib and carfilzomib) and IMiDs (ie, thalidomide, lenalidomide, pomalidomide).[24,30] Monoclonal antibody therapies such as elotuzumab and daratumumab are currently being evaluated in clinical trials for the treatment of MM.[31,32]

Changes in MM management, including the use of high-dose therapy, stem cell transplants, and novel agents, have resulted in an increase in median survival. Compared with patients who received a diagnosis of myeloma between January 1971 and December 1996, those who received a diagnosis between January 1997 and December 2006 had a significant improvement (50%) in overall survival (44.8 months vs 29.9 months; P <.001).[5] Furthermore, 10-year survival in patients with MM is highest in younger patients and decreases as age increases.[33] However, in late-line patients, defined as those with International Stating System Stage II or III disease with more than 1 adverse lesion, the median overall survival is 19.4 months and progression-free survival is 9.9 months.[11]

In patients with active MM, initial treatment consists of primary therapy that may or may not be followed by high-dose chemotherapy with autologous stem cell transplant depending on their eligibility and other considerations such as presence or absence of symptoms, disease stage, age, comorbid conditions, and response to treatment.[24]

In addition to conventional treatments and transplant, other treatments include adjunctive treatments, supportive

care, and clinical trials. Adjunctive care includes bisphosphonates for bone disease; prophylaxis for infections; low-dose radiation for uncontrolled pain or for impending pathologic fracture or cord compression; plasmapheresis for symptomatic hyperviscosity; colony-stimulating factors and erythropoietin for anemia; and anticoagulation for thrombotic event management.[24]

At this time, unmet needs in the field of MM include a need for more treatment options in extramedullary disease, relapsed or refractory disease, and those with high-risk cytogenetic profiles. More data from prospective trials are also needed regarding the effectiveness of stem cell transplants versus other therapies and the most effective combinations of medications for high-risk, medium-risk, and standard-risk patients.

Treatment Costs

There is a growing concern that patients are increasingly unable to afford cancer treatments based on a number of factors, including longer lifespans, large deductibles that lead patients to pay large out-of-pocket costs before receiving an insurance benefit, and high costs of coinsurance and copays.

Patients may not discuss their financial concerns with their healthcare providers. A preliminary analysis of data from the Cancer Support Community Cancer Experience Registry: Multiple Myeloma indicated that 19% of the respondents reported that they had discussed the impact of MM on their personal finances with their healthcare team, and that 84% reported that financial counseling would help "quite a bit" or be "very helpful" to someone with multiple myeloma. Half (50.8%) of the respondents reported that a member of their healthcare team talked to them about resources related to getting financial help or financial counseling.

The roundtable participants noted that costs may affect adherence to treatment regimens and that assisting patients with treatment reimbursement issues is costly for providers.

Evolution of Treatment of MM

Over the last 10 years, MM has evolved into a chronic disease; many patients are now living with MM for a decade or more.

PART II

Managed Oncology: A Pathways Model for Efficient, High-Quality Care

Cancer remains a significant healthcare challenge from both a cost and a quality-of-care point of view. According to the National Cancer Institute, the cost of cancer care was $157 billion in 2010, and is projected to be $174 billion by the year 2020, with the bulk of costs driven by care delivered during the diagnosis and end-of-life phases.[34] Cancer is associated with an estimated cost of approximately $900 billion in disability-adjusted life-years (ie, costs attributed to years lost from ill health, disability, or early death). The costs of cancer are increasing rapidly due to several factors, including aging and expanding populations, the rapid development of new medicines and surgical techniques, and increasing healthcare expenditures.[35] With regard to MM, the costs of MM account for almost 9% to 10% of total cancer care costs; this is highly disproportionate to the incidence and prevalence of MM relative to other tumor types.

Optimizing the delivery of cancer care is challenging because community practice economics are changing, with lower reimbursements for services and rising administrative costs. Some of the potential ways to reduce the cost of care include promoting the use of evidence-based medicine, educating providers and patients about value-based care, implementing integrated care delivery systems, defining value-based approaches in cancer care, and applying value-based pricing determined by comprehensively evaluating outcomes and costs of treatment approaches or modalities.[35]

Defining Value

Stakeholders in the healthcare marketplace may have varying and conflicting goals. One potentially unifying goal is achieving high value, with value defined in terms of health outcomes per dollar spent.[36]

Defining Measures of Quality Healthcare

Efforts to reduce costs and improve healthcare outcomes must begin with an examination of quality measures and

their improvement in the setting of oncology practices, including MM. Quality practices and processes should be based on the efficient use of evidence-based medicine through a platform that provides content and work flows that can be integrated into payer (ie, managed care organization) and provider systems to simplify the administrative processes for providers. Such systems must avoid waste and misuse of medical services by improving provider alignment (ie, primary care physician, medical oncologist, surgeon), using more defined networks, and implementing the consistent use of strong decision-support strategies. Quality cancer care systems must also leverage and integrate the many current and future medical and pharmacy cancer care initiatives into a seamless, end-to-end cancer experience for patients and providers.[37]

Improved Collaboration Is Key

Participants noted that there are many factors in the total continuum of care that could be better managed if there were improved collaboration between key stakeholders including healthcare professionals, the pharmaceutical industry, managed care, and the US government (eg, CMS).

To develop meaningful measures of quality, the definition of a good measure must first be explored. According to the National Quality Measures Clearinghouse (a US Department of Health and Human Services initiative to define quality care), a measure must be important, scientifically sound, and feasible. The importance of the measure is defined by its relevance to stakeholders including patients, clinicians, and purchasers. Measures may evaluate processes, structure, or outcomes. Scientific credibility is a necessary component that relies on explicit support from evidence-based improvements in the quality of care or health outcomes. Of course, good measures are also defined as those that are reproducible, are backed by validity testing, allow for stratification, and are easily understood by the person who will be acting on the measure outcome. Finally, the evaluation of measures must be feasible, with data collection methods that are understandable and usable, and costs that are justified by the potential for improvement in care or health.[38]

Several questions may be asked to define a good measure of process, structure, or outcomes, including[38]:

1. How strong is the scientific evidence supporting the validity of this measure as a quality measure?
2. Is the result of the measure under the control of those whom the measure evaluates?
3. How well do the measure specifications capture the event that is the subject of the measure?
4. Does the measure provide for fair comparisons of the performance of providers, facilities, health plans, or geographic areas?
5. Does the measure allow for adjustment to exclude patients with rare performance-related characteristics when appropriate?

At this time, several healthcare-focused organizations are engaged in measuring the quality of oncology healthcare; these groups include the National Quality Forum, the Quality Oncology Practice Initiative (a program from the American Society of Clinical Oncology), the Consumer Assessment of Healthcare Providers and Systems, the National Committee for Quality Assurance, and the Community Oncology Alliance (COA).[37,39-43]

Improving Value in the Healthcare Market

In addition to measuring the quality of healthcare, current trends in the managed care market also include a focus on value and strategies for containing costs without compromising care. One essential aspect of cost savings involves measuring variation in total cancer costs because the costs of various cancer therapies often differ substantially. For example, in non-small lung cancer, the cost of 6 cycles of Alimta plus cisplatin is $33,278, more than 10-fold higher than 6 cycles of carboplatin plus paclitaxel ($2047). Likewise, in colon cancer, 8 cycles of Xeloda plus Eloxatin costs $45,877, compared with 6 cycles of fluorouracil/leucovorin/Eloxatin, which costs $34,687. The development and approval of additional therapies will change the treatment landscape. According to Dr Klein, aside from prescription drugs, other costly aspects of care

Incorporating Rapidly Changing Treatment Strategies

Concerns were voiced about how to build rapidly changing treatment strategies into the platform of a guideline/pathway, a task that may be especially difficult for those who are not healthcare providers.

include inpatient hospitalizations, emergency department (ED) visits, and radiology.[37]

To achieve value within the healthcare marketplace, quality must be increased using effective strategies to minimize costs. Increased quality can be achieved by many methods, including the use of guideline-based therapy, targeted therapies, and treatments that have been associated with low toxicity, higher survival, and better quality of life. Furthermore, costs can be decreased by using appropriate supportive care strategies, avoiding hospitalization and ED visits, decreasing site-of-service costs, and reducing the use of medically unnecessary care at the end of life.[37] The results of a recent study suggested that adherence to treatment guidelines can significantly lower costs without impacting efficacy (ie, no change in overall survival between study groups). The study was conducted to evaluate the cost-effectiveness of using evidence-based Level 1 Pathway recommendations for patients with non-small cell lung cancer. Use of the Level 1 Pathway encourages the consistent delivery of value-driven, evidence-based treatment with a goal of delineating treatment options that maximize survival, minimize toxicities, and provide cost-saving advantages. The study was retrospective in nature and evaluated patients treated at 8 different cancer centers in the United States over an 18-month period. Patients were classified as treated on or off pathway; those who were treated both on and off the pathway were excluded. Cost driver analysis was conducted by breaking costs down into several categories including outpatient visits, medications, laboratory services, and ancillary services, and 12-month survival was compared using the Kaplan-Meier method and corresponding log-rank test. The study found that high-quality therapy supported by evidence-based guidelines was not high in costs, especially in patients who were receiving first- and second-line therapy.[44]

Clinical Pathways to Improve/Maintain Outcomes and Streamline Costs

The use of a clinical pathway is helpful in providing a treatment road map of best care practices. Such pathways are developed based on an evaluation of research and medical evidence, including comparisons of efficacy, toxicity, and costs. Lines of therapy in a given pathway describe drug combinations and sequences that are recommended based on evaluation of evidence. The suitability of treatment initiation and discontinuation is described, and new lines of therapy are often added when another has not met a clinical outcome or when cancer progresses.[37]

The Value of Clinical Pathways

A hidden value of clinical pathways and the reason for their importance is that the use of a systematic resource with rules allows for the measurement of outcomes/effects to guide future practice.

Clinical Pathways and Reimbursement

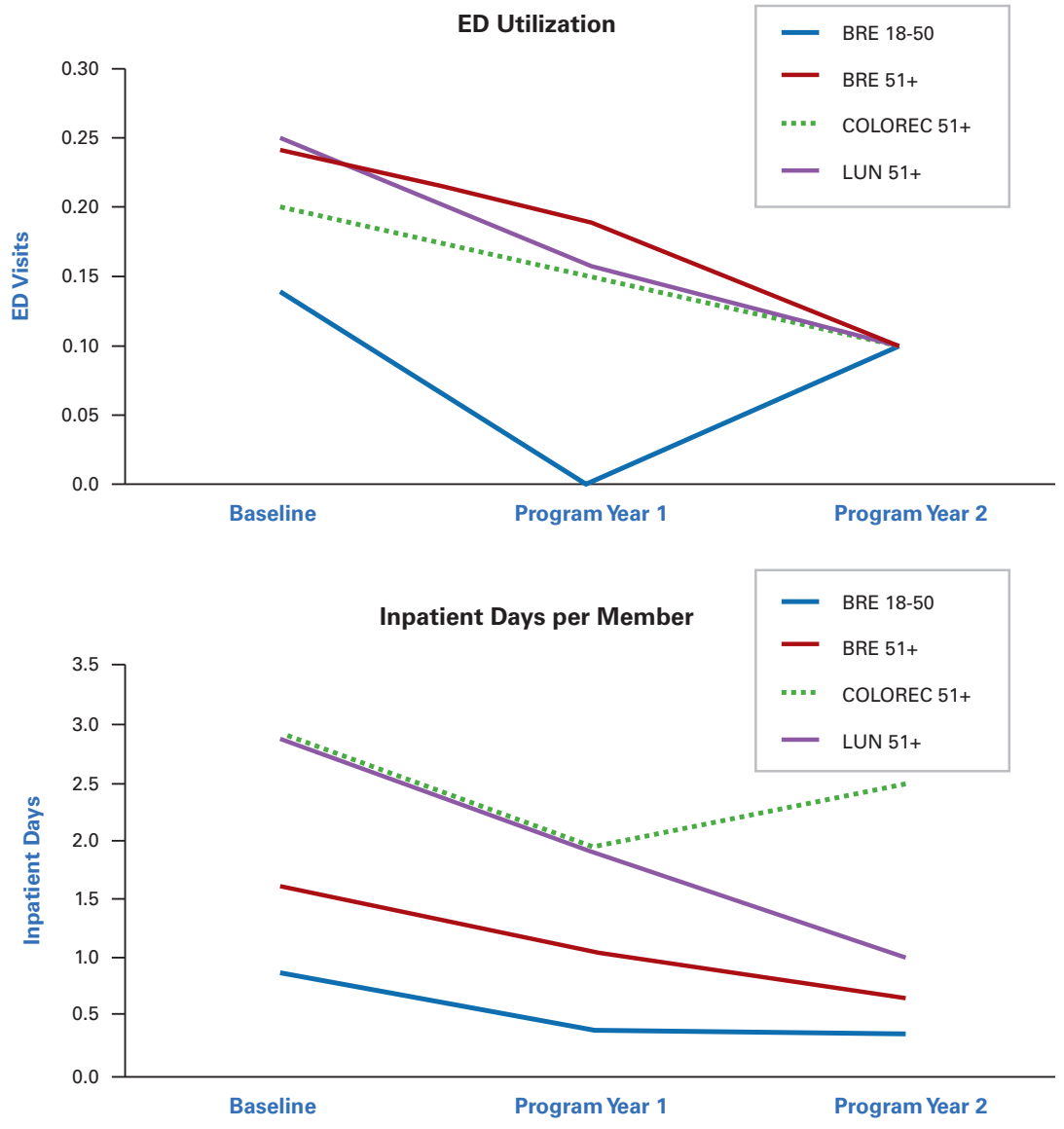
Many participants were concerned about reimbursements and fairness in clinical pathways; the key to promoting the adoption of guidelines is to reimburse for services that are incorporated in the guidelines, to develop fair balance in pathways, and to address the challenge of how to best incorporate newer agents in rapidly changing treatment landscapes.

Pathways and MM

Although a clinical pathways program for MM doesn't exist yet, it was discussed that a program such as this might be beneficial because MM has evolved from an acute to a chronic disease, and as such, costs will continue to increase as patients with MM are surviving longer and requiring continual care during remissions and relapses. Also, the treatment landscape is still evolving and new options (and guidelines) are forthcoming. For example, NCCN guidelines allow a lot of flexibility in prescribing. Clinical pathways may help reduce costs by using an evidence-based approach that is in line with guidelines, which may reduce local, regional, and national variations in practice.

A pilot clinical pathway program called P4 Pathways has been developed to provide consistent, high-quality, cost-effective care to oncology patients in several states (including Maryland, Virginia, Florida, Pennsylvania, and Michigan) and Washington, DC. At this time, 156 physicians are participating in the program; both fully insured and self-insured customers are participating. In the P4 Pathway, Aetna physicians identify clinical protocols to

Figure 1. Cost Savings for Patients Enrolled in Innovent Model Pathway[37,45,46]



BRE indicates breast cancer; COLOREC, colorectal cancer; ED, emergency department; LUN, lung cancer.

improve consistency, quality, and the cost efficacy of treatments for breast, lung, colon, and other common tumor types. The P4 Pathways program also provides tools and proprietary technology to train physicians who are within the Aetna network to implement and adhere to the pathways. The tools are used to capture clinical results and track cost savings of the pathway program without burdening the provider with the need for additional administrative work.[37]

At this time, the P4 pilot program has evaluated the distribution of patients according to cancer diagnosis and also the lines of therapy used for these patients. Of 86 patient-lines of therapy initiated, 44 were in breast cancer, 30 were in lung cancer, and 12 were in colon cancer.

The findings of the pilot P4 program have revealed that by using the pathway, treatment variability was reduced by 28% (ie, the number of distinct drug regimens was reduced by 15); before the program, the number of distinct drug combinations used was 53 compared with 38 during the program year. Furthermore, generic-only utilization increased by 11%; prior to the implementation of the P4 Pathway, 63% of patients used generic-only treatments compared with 70% of patients who used generic-only treatments during the program implementation. Of note, Aetna has reported that brand-containing regimens cost approximately $68,000 versus $13,000 for a comparable generic regimen.[37]

Innovent Oncology, a subsidiary of US Oncology, one of the nation's largest networks of integrated, community-based oncology practices, implemented a similar program in 2010 called the Innovent Oncology Program. This program deployed a pathways approach through proprietary desktop software integrated into the office electronic medical records system, as well as "patient support services," a set of care management protocols designed to educate, inform, and guide patients through active treatment. A prospective, non-randomized study evaluated the impact of this pilot program on compliance and cost savings[37] and found that 76% of all participants complied with the pathway whereas 24% did not and 4% were non-assessable. Similar to the results of the P4 pilot, the Innovent Program resulted in a 12% overall cost savings in breast, lung, and colon cancer patients based on decreased ED utilization and fewer inpatient days (**Figure 1**).[37,45,46] The P4 pilot and the Innovent Program are examples of the implementation of the pathways approach; various payers are currently developing and implementing other oncology-specific pathways and decision tools.

The benefits of a clinical pathway are not restricted to payers; healthcare consumers may benefit through improved health outcomes (as a result of improved care management and adherence to evidence-based guidelines), reduced hospitalizations and ambulatory care, improved transitions of care, and increased shared decision making and engagement in preventive health and wellness.[37]

One recent example of a new economic model in cancer care is the oncology medical home (OMH). The basic components of an OMH include coordination of care and easy access to care; case management responsibilities; improved tracking of medication compliance and follow-up; reporting capabilities; and enhanced communication/patient education. Measurements of quality that are followed within the OMH model include the percentage of adherence to clinical pathways, the number of patients with documented staging prior to treatment, ED visits and hospital admissions per patient year, patient deaths occurring in an acute setting, average days in hospice prior to death, and percentage of patients with stage IV cancer that have end-of-life discussions. Barriers to the implementation of new models such as the OMH model exist; interviews conducted with community-based oncologists suggest that many providers lack the knowledge and finances to adopt new models.[37] The OMH model and its benefits are discussed in further detail in Part III of this article.

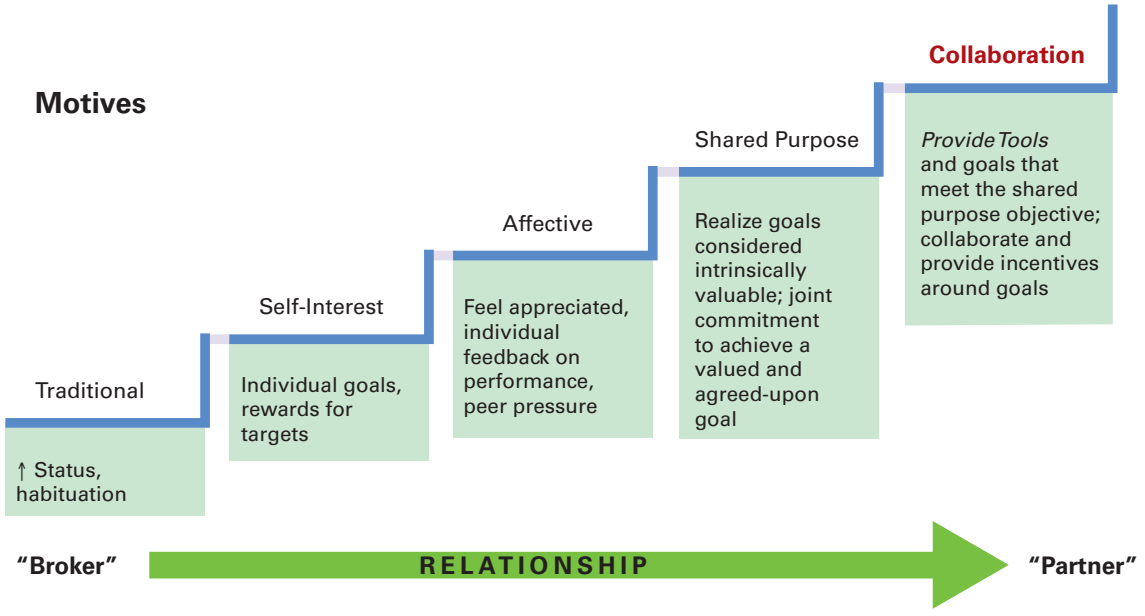
Clinical Pathways, the OMH Model, and MM

Thus far, programs involving clinical pathways and the OMH model have been implemented in the treatment of breast, colon, rectal, and lung cancer, due to the larger patient populations. As more experience is gained with clinical pathways and the OMH model, these strategies may also be applied to the management of MM.

A Dynamic Reimbursement Paradigm

At this time, several promising strategies are being implemented to improve quality of care and value in the healthcare setting. A number of factors are contributing to shrinking reimbursements, including a changing reimbursement mix that is becoming dominated by Medicare and Medicaid, federal pressures (passage of the Affordable Care Act), and state budget deficits. Furthermore, the shift from fee-for-service to value-based payment models is changing the risk profile of cancer management. While traditional models such as fee-for service and pay-for-performance increase payer risk, evolving payment mechanisms such as the OMH and value-based payments increase provider risk. As a result, new physician-payer collaborations are forming to temper risk. For example, to improve payer-provider relationships, there is a need to define a shared purpose among oncology care collaborators. To this end, the use of ethical physician incentives will allow the relationship of the payer to evolve from one of broker to that of a partner (**Figure 2**).[37,47]

Figure 2. Challenges in the Establishment of Payer-Provider Relationships[37,47]



PART III

The Implications of Newer Payment and Practice Models

As discussed in Part II, major changes are under way for all stakeholders in the healthcare arena, including payers, providers, and patients. A variety of factors have contributed to the need for healthcare restructuring, including increasing medical costs, decreasing payer reimbursements, and mandates of federal healthcare reform such as the Affordable Care Act of 2010. In an effort to address many of these issues, several strategies have been suggested, including the use of value-based reimbursements in place of fee-for-service care; the use of coordinated care models to improve efficiency, reduce drug costs, and decrease the likelihood of duplicating costly testing and other services; and the use of clinical pathways to standardize treatment approaches. Although these strategies have not yet been attempted in MM, it is thought that the use of a clinical pathway may facilitate the use of guideline-recommended strategies to improve outcomes, decrease costs, and possibly streamline treatment.

Drivers of Quality-Based Change

In the United States, the federal government is the single largest purchaser of healthcare (eg, via Medicare, Medicaid, and the Veterans Health Administration).[48] To maintain the viability of government-backed healthcare reimbursements, a lifeline to affordable medical care for many Americans, recent efforts have focused on improving quality and efficiency in the healthcare marketplace. Based on these needs, a number of drivers have been put in place by CMS to coordinate patient care and to evaluate quality from the perspective of both the payer and the consumer (ie, the patient).

CMS has contracted with several types of accountable care organizations (ACOs), which are defined as groups of doctors, hospitals, and other healthcare providers who voluntarily join forces to provide high-quality care to Medicare patients. The goal of this organized care approach is to ensure that patients receive the right treatment at the right time while avoiding unnecessary duplication of services and preventing medical errors. If the ACO reduces costs relative to projected levels, the ACO receives a portion of the savings. At this time, Medicare offers several ACO programs including a Medicare Shared Savings Program (a program that helps Medicare fee-for-service provider become an ACO), the Advance Payment ACO Model (a supplementary incentive program for selected participants in the Shared Savings Program), and the Pioneer ACO Model (a program designed for early adopters of coordinating care; applications are no longer being accepted for this program). For organizations wishing to learn more about ACO programs, the CMS offers an ACO Accelerated Development Learning Sessions. Of note, participation in an ACO is purely voluntary.[49] Currently, CMS has begun implementing a plan to report quality-of-care data, as required by the Affordable Care Act. In 2014, CMS will begin posting the first set of data from the ACOs and also the Physician Quality

Reporting System (PQRS), a pay-for-reporting system that rewards satisfactory reporting by providing incentives and payment adjustments.[50]

As part of a program that rewards value rather than volume, CMS has developed The Physician Feedback/Value-Based Payment Modifier Program. The program was designed to provide physicians and group practices with feedback in the form of data on comparative measures. Using this feedback, the goal is to allow healthcare providers to improve their quality of care and increase efficiency. The Physician Feedback/Value-Based Payment Modifier Program comprises 2 components, the Physician Quality and Resource Use Reports (QRURs) (also known as "The Reports") and the development and implementation of a value-based payment modifier. The program was developed to help transform Medicare from a passive payer to an active purchaser of higher-quality, more efficient healthcare through value-based purchasing initiatives. Legislation that called for the provision of feedback to physicians included Section 131 of the Medicare Improvements for Patients and Providers Act of 2008, and section 3003 of the Affordable Care Act of 2010, which directed CMS to provide information to physicians and medical practice groups about the patterns of resource use and costs and quality of care provided to their Medicare Fee-For-Service patients. Most resource use and quality information in the QRURs is displayed as relative comparisons of performance among similar physicians or groups. By 2015, the Affordable Care Act mandates that CMS must apply a value modifier under the Medicare Physician Fee Schedule (MPFS) with both cost and quality data to be included in calculating payments for physicians. By 2017, the Value-based Payment Modifier is to be applied to all physicians who bill Medicare for services provided under the physician fee schedule. The QRURs are being piloted in 9 states (California, Illinois, Iowa, Kansas, Michigan, Missouri, Mississippi, Wisconsin, and Nebraska).[51]

Recently, the Physician Compare program (www.medicare.gov/physiciancompare) was developed as a requirement of the Affordable Care Act of 2010 to provide consumers with information that will help guide their healthcare decisions and to create incentives for physicians to maximize service to patients. At this time, information available on the Physician Compare site includes healthcare professionals' names, addresses, and phone numbers; information regarding clinical training, specialties, and languages spoken by physicians; physician hospital affiliations; and practice-specific Medicare-approved amounts accepted. Also included is group practice information such as address, phone number, and a list of physicians who provide services at each practice.[50] Another tool developed for patients is called Hospital Compare (www.hospitalcompare.hhs.gov), which was designed to provide a measure of quality from the consumer's point of view. The purpose of the Hospital Compare website is to rate and report hospital care that has been provided to patients in an effort to help consumers make better-informed decisions about medical care. Using the Hospital Compare website, consumers are able to select multiple hospitals and compare performance information based on their selected medical condition. Some of the data that the patient surveys evaluate and describe include ratings of timely and effective care; the number of readmissions, complications, and deaths; the use of medical imaging; Medicare volume; and linking quality to payment. Hospital Compare was created in 2002 through Medicare and the Hospital Quality Alliance. In 2013, Hospital Compare will include data on the new Hospital Value-Based Purchasing program.[52]

The common theme among all the aforementioned programs is that they utilize well-defined, measurable benchmarks of achievement or quality to evaluate healthcare. Strategies for healthcare reform are being led by all participants, including patients, payers, and providers, and are based on meaningful measurements. To streamline costs, it is imperative that these initiatives not cause significant administrative or financial burden to providers. The goal of these initiatives is to benchmark through quality and to reimburse providers based on quality and value.

The Community Oncology Alliance and the Oncology Medical Home

The COA is a nonprofit organization that is dedicated to providing proactive solutions to protect care delivery systems in the community oncology setting, where the majority of Americans with cancer are treated. Over the past 10 years, the COA has become more politically active in Washington, DC, with the goal of increasing awareness with regard to community care delivery. Aside from its political involvement, the COA has also played an integral role in the dissemination of cancer information by gathering community oncologists from across the country. At this time, the COA is working with Congress to provide proactive solutions that will protect the viability of the nation's cancer care system and protect access to quality, affordable healthcare.[42]

Based on the need to improve patient focus and evaluate measures of quality and value in the community oncology care setting, the COA began developing an initiative to form an OMH, a specialized type of medical home. The medical home model has been in existence for more than 40 years. The purpose of a medical home is to provide coordinated

care using a "gatekeeper" or "coordinator," typically the primary care physician, to oversee both primary and specialty care, with the intention of streamlining costs, improving patient satisfaction, and ultimately resulting in more favorable outcomes. In oncology care, the OMH uses a specialty physician—the oncologist—as the primary gatekeeper or coordinator of care. There are several reasons why the oncologist serves as the primary caregiver in a disease state such as cancer. Most of these reasons relate to the complexity of cancer treatments and the management of associated symptoms. Furthermore, most primary care physicians are not trained to administer chemotherapy or radiation and do not have the necessary experience to manage serious side effects of cancer treatment. It is hoped that optimal cancer management through the use of an OMH will reduce the incidence of costly ED visits and hospitalizations.[48]

The Need for Improved Communication

Unmet needs in the current management of MM noted by participants included care coordination, collaboration among stakeholders, and plan communication. The OMH may have a tremendous impact by helping to streamline/improve communications between healthcare providers and patients, thus eliminating extra costs due to inefficient communication.

Evidence Regarding Communication Gaps

A preliminary analysis of data from the Cancer Support Community Cancer Experience Registry: Multiple Myeloma indicated that one-third of respondents reported that they mentioned the full extent of their side effects and symptoms to their healthcare team never, rarely, or sometimes.

The OMH model has been supported by 2 reports by the Institute of Medicine (*Ensuring Quality Cancer Care* and *Assessing* and *Improving Value in Cancer Care*). One of these reports established the following components/processes of care as essential in the management of patients with cancer[48]:

- Use of standardized evidence-based guidelines for prevention, diagnosis, treatment, and palliative care
- Measurement and continuous monitoring of a core set of quality measures
- Agreed-upon care plan prepared by experienced professionals, outlining the goals of care
- Access to clinical trials
- Policies to ensure full disclosure of information to patients about appropriate treatment options
- Mechanisms to coordinate services
- Quality care at the end of life
- Policies addressing the barriers to receiving appropriate cancer care in specific segments of the population

The OMH Model and MM

Medical homes are designed to provide comprehensive care to patients with chronic conditions, with a focus on patients and the entire treatment continuum. MM has evolved from an acute disease to a chronic disease, making the OMH well suited for the management of MM. However, a challenge for use of this model in MM is incorporation of the proliferation of new treatments and standardization of the various treatment approaches, specifically with regard to aggressiveness and the duration of treatment, which often differ by provider.

Thus far, the OMH model has been applied in the treatment of breast, colon, rectal, and lung cancer, due to the larger patient populations. As more experience is gained with the OMH model, this model may also be applied to the management of MM.

At the start of the project, the COA determined that the stakeholders, including patients, payers, and providers, must lead the initiative. Ideally, according to the research conducted by the COA, the strategy to build an OMH must include meaningful measurements, require minimal administrative support/finances, have the ability to analyze benchmarks according to quality, and pay for achievements in quality and value. Therefore, to begin development, the COA assembled a Steering Committee that included oncologists, administrators, cancer care advocates, payers, and a patient, nurse, pharmacist, and business partner. The committee has been instrumental in structuring the OMH by

Table 3. Comparison of Stakeholder Needs[53]

Patients	Payers	Providers
• Best possible outcome • Doctors with the 3 A's (Able, Affable, Accessible) • Least out-of-pocket expense • Education and engagement of the patient in the care plan • Best quality of life	• Best possible clinical outcomes • Member satisfaction/experience • Control total costs/variability • Productivity/survivorship • Meaningful proof of quality/value	• Best outcome for patient • Satisfied patients and family • Fairest reimbursement to provide quality patient care • Compensated for cognitive services, including treatment planning, end-of-life care, and survivorship • Fewer administrative burdens

Table 4. Components of Meaningful Measurement Including Quality, Value, and Outcomes[53]

Patient Care Measures
• Received a treatment plan prior to the administration of chemotherapy, patients (%)
• Had documented clinical or pathologic staging prior to initiation of first course of treatment, patients (%)
• Chemotherapy treatments adhered to NCCN guidelines or pathways, %
• Antiemetic drugs given appropriately with highly emetogenic chemotherapy treatments
• Received GCSF/white cell growth factor following a chemotherapy regimen associated with ≥ 20% of neutropenia, patients (%)
• Management plan included appropriate use of advanced imaging for early-stage breast cancer patients
• Management plan included appropriate use of advanced imaging for early-stage prostate cancer patients
• Presence of patient performance status prior to treatment
Resource Utilization
• Number of emergency department visits per chemotherapy patient per year
• Number of hospital admissions per chemotherapy patient per year
Survivorship
• % of cancer patients that received a survivorship plan within X days after the completion of chemotherapy
• % of chemotherapy patients that received psycho/social screening and received measurable interventions as a result of the psycho/social screening
• Survival rates of stage I through IV breast cancer patients
• Survival rates of stage I through IV colorectal cancer patients
• Survival rates of stage I through IV NSC lung cancer patients
End of Life
• % of patients that have stage IV disease that have end-of-life care discussions documented
• Average number of days under hospice care (home or inpatient) at time of death
• % of patient deaths where the patient died in an acute care setting
• A measurement of chemotherapy given near end of life

GCSF indicates granulocyte colony stimulating factor; NCCN, National Comprehensive Cancer Network; NSC, non-small cell.

identifying the needs of patients, providers, and payers in the delivery of cancer care. Interestingly, a survey conducted by the COA to determine stakeholder needs revealed that all stakeholders had similar interests (ie, evidence-based medicine, a good experience, controlling cost or the variability of cost, survivorship, and meaningful quality of life) (Table 3).[53]

To develop the new practice model, many measures of quality and outcomes were eventually streamlined. Following the development of the measures, a registry concept was designed that included data points to report outcomes. After the identification of stakeholder needs, the committee worked together to identify and eventually endorse a set of quality and value measures of cancer care (Table 4).[53] Additionally, the committee backed the development of a patient satisfaction tool, based on a modification of the Consumer Assessment of Healthcare Providers and Systems survey tool, which was developed by the AHRQ to assess consumer experiences with healthcare.

One goal of the OMH model is to provide automatic real-time measures for providers to stimulate improvement. Although payment will not be tied to patient satisfaction, the hope is that providers will strive for improved scores after reviewing patient satisfaction reports. However, the model pays for performance that is above average, with higher rewards for higher performance. Furthermore the COA has appointed an Implementation Team to identify the information and tools needed by community oncologists to transform into a fully functioning OMH. To date, the team has identified over 50 such tools and is working to produce a tool kit that is customizable according to level of sophistication.[48]

The COA is currently in discussions with the Commission on Cancer (CoC) to construct a method of capturing these data points to define optimal treatment pathways. The CoC is a consortium of professional organizations dedicated to improving the survival and quality of life of cancer patients through education, research, and monitoring comprehensive quality of care.[54] The CoC is actively and aggressively pursuing a data registry for OMHs that includes the automatic extraction of outcomes data from an automated master cancer database with billing based on the summation of data measures.

In summary, this model aims to provide automated reporting of 19 OMH measures of value/quality and incorporates OMH accreditation with the CoC. Measuring and reporting are thought to cause natural positive improvement along with payment incentives associated with the reporting of each measure to compete for high positioning within each measure. The use of an OMH is hoped to alleviate some of the challenges that community oncology practices are faced with by streamlining care and providing guidelines to participate in value-based reimbursement. It is hoped that this model will both improve care in the field of oncology and provide cost savings without compromising outcomes; however, the optimal method of measuring quality and constructing a high-quality and productive OMH may be subject to debate.

OMHs: Many Questions Remain

There are many outstanding questions regarding the successful implementation of an OMH, including the measures to be included, the incentives for performance, the need for pharma involvement, how to address the issue of increased costs for provider implementation, and whether the OMH model can be successful when applied to the management of patients who may potentially undergo many years of treatment.

Summary

With advances in treatment, the overall survival of patients with MM has improved, and MM has evolved into a chronic disease. Together with the high total costs of MM, which are highly disproportionate to its incidence and prevalence, the chronic nature of MM calls for a more optimal care delivery system. However, optimizing care delivery is challenging in oncology community practices due to changes that include lower reimbursements for services and increasing administrative costs. One potential solution includes the use of clinical pathways to reduce costs by adhering to an evidence-based approach to treatment and by reducing variations in clinical practice. Although a clinical pathways program for MM does not exist at this time, a program such as this might be beneficial in MM because costs will continue to increase as patients with MM are surviving longer and requiring continual care during extended periods of continued remissions and relapses. However, challenges to the implementation of such a pathway include the ever-changing treatment landscape in MM, which is always evolving with new treatment options (and guidelines) continually forthcoming. For example, NCCN guidelines allow a great deal of flexibility in prescribing. Another possible solution to decrease costs and streamline care in MM involves the use of a medical home model, which is designed to provide comprehensive care to patients with chronic conditions. Because MM is frequently chronic, the OMH may be well suited for the management of MM. The goal is to provide more coordinated care and decreased costs by avoiding duplication of services. Furthermore, with the oncologist as the primary gatekeeper, it is hoped that adverse events, hospitalizations, and ED visits will be reduced and patient outcomes will be improved.

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