The Continuum of Care in Multiple Myeloma Redefined: Challenges and Opportunities

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Author's disclosures of potential conflicts of interest are found at the end of this article

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Continued advances in the diagnosis, risk stratification, treatment, symptom management, supportive care, and foundational basic sciences relative to multiple myeloma (MM) over the last decade are staggering. The improvement in survival rates in both newly diagnosed and relapsed patients treated with novel agents over the last two decades is equally impressive. There has been a doubling of survival in patients treated at the time of relapse after the year 2000 (Kumar et al., 2008), a 50% improvement in overall survival in patients newly diagnosed after the year 2000 when compared to the previous two decades (Kumar et al., 2008), and a 92% improvement in survival rates (3.8 vs. 7.3 years) when comparing patients treated from 2001 to 2006 with those treated from 2006 to 2010 (Kumar et al., 2012).

The foundation of these improvements in survival has been provided by ongoing clinical trials using novel agents, including immunomodulatory agents and proteasome inhibitors. More recently, new classes of drugs, including histone deacetylase inhibitors, oral proteasome inhibitors, and monoclonal antibodies, have gained approval for use in expanding treatment options for MM patients. In addition, refinement of dosing, administration techniques, treatment schedules, and sequencing for existing agents have demonstrated improved efficacy and improved tolerance and safety, which in many cases have translated into a longer duration of response (Benboubker et al., 2014; Kurtin, Knop, & Milliron, 2012; Rajkumar et al., 2010; Richardson et al., 2010).

More recently, data suggest that patients who have no evidence of minimal residual disease after induction therapy, which is then sustained for a period of years, may enjoy prolonged survival and perhaps even have hope for a cure (http://bsri.myeloma.org). As a result, achieving an early and deep response—with incorporation of autologous stem cell transplantation in eligible patients, use of maintenance therapies when indicated, and treatment until disease progression or unacceptable toxicity—has become a core principle in the treatment of MM (Baz et

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al., 2013; Ludwig et al., 2014; Mikael et al., 2013; NCCN, 2016; Palumbo et al., 2013; Palumbo et al., 2014; San Miguel, 2014). The diagnostic criteria and disease nomenclature for MM have recently changed, incorporating refined criteria and identifying patients with asymptomatic myeloma who may benefit from earlier treatment that could prevent end-organ damage (Rajkumar et al., 2014). This shifting treatment paradigm has implications for patients, caregivers, and providers across the continuum of care (Figure 1, Table 1).

Amidst all of these positive developments, delivering or receiving cancer care has become increasingly complex. There are a growing number of regulatory and quality measure outcomes mandated by the Institute of Medicine (IOM), the Affordable Care Act (ACA), the Commission on Cancer, and insurance reimbursement policies (Table 2). Integration of the ACA includes the incentive program for meaningful use (MU). The MU program is based on the premise that simply adopting and documenting in an electronic health record (EHR) is not sufficient to improve patient outcomes (Blumenthal & Collins, 2010). Rather, utilizing the EHR to improve individual and population-based initiatives across health care settings, evaluating patient-reported outcomes (PRO), engaging the patient in their care, and implementing continuous quality improvement initiatives (CQI) using aggregate data is required. Expanded access to health care through the ACA is a key impetus for the Health Information Technology Act (US Department of Health and Human Services, 2010). The major coverage provisions of the ACA went into effect in January 2014, with an estimated 8 million new covered lives by 2015 and an estimated 25 million total covered lives by 2017 (Blumenthal & Collins, 2010). Universal use of fully integrated EHR technology is considered critical to effectively managing the anticipated increased number of patients actively engaged in the health care system (Blumenthal & Collins, 2010).

Cancer survivors are projected to exceed 19 million by 2024 (American Cancer Society, 2014), yet there is an anticipated shortfall of oncology providers, especially practicing oncologists (ASCO, 2015). Effectively integrating regulatory and quality requirements while simultaneously applying principles of risk-adapted therapy in the era of a digital world presents a number of challenges for MM patients, their caregivers, and health care professionals. Adding to the complexity, the majority of MM care is provided in an outpatient, setting placing the bulk of responsibility for day-to-day care on the patient and their caregivers (Kurtin, Lilleby, & Spong, 2013).

With the improvement in survival and overall clinical outcomes for MM survivors, the concept of MM as a chronic disease has been suggested. Common to most chronic diseases, the challenge of extended treatment over time to effectively control the disease places demands on the patient, their caregivers, health care providers, and the health care system. The goals are to optimize outcomes and improve quality of life (QOL). Periods of transition, such as diagnosis, progres-

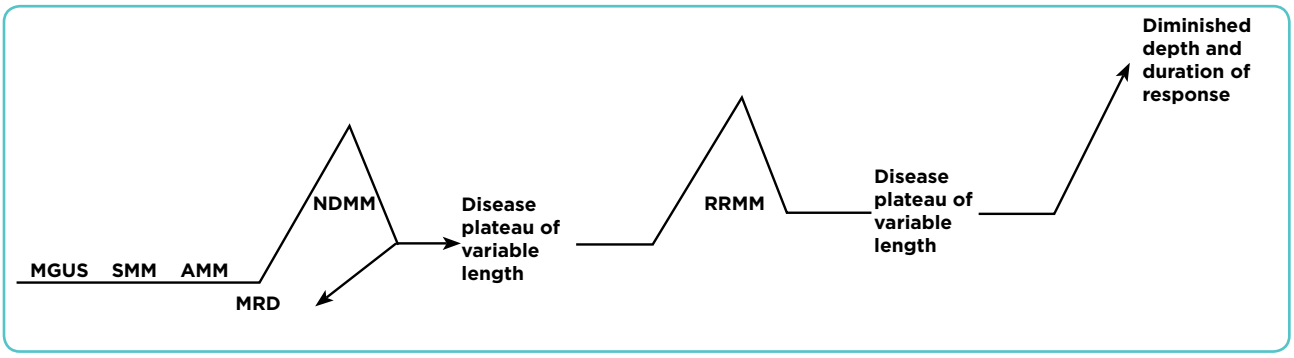

Figure 1. Multiple myeloma disease trajectory. MGUS = monoclonal gammopathy of uncertain significance; MM = multiple myeloma; SMM = smoldering MM; AMM = asymptomatic MM; NDMM = newly diagnosed MM; MRD = minimal residual disease; RRMM = relapsed and/or refractory MM. Adapted with permission from Durie et al. (2003).

Table 1. Clinical Strategies, Supportive Care, and Survivorship Across the Multiple Myeloma Continuum of Care

	MGUS	SMM	NDMM	RRMM
Disease characteristics	Risk of transformation to MM = 1%/yr	Risk of transformation to MM = 10%/yr Absence of MDE	• Clonal plasma cells > 10% or biopsy-proven bony or extramedullary plasmacytoma • Presence of MDE as defined by IMWG criteria • Any one or more of the following: ○ BMPC > 60% ○ Involved/uninvolved serum free light chain ratio > 100 ○ > 1 focal lesion > 5 mm on MRI studies	• Meets IMWG criteria for progressive disease • Each episode of relapse is generally associated with a shorter duration and depth of response
Clinical strategies	Risk stratification Surveillance Supportive care		• Risk-adapted treatment selection: Evaluation of comorbidities, fit vs. frail, elderly vs. young • Consideration of clinical trials and evaluation for transplant eligibility • Advance care planning • Supportive and palliative care • Caregiver support	
Goals of care	Early identification of high-risk disease		• Initiation of the best available treatment to induce an early and deep response • Limit end-organ damage • Maintain a durable response by optimizing each treatment option to achieve MRD • Use of AHSCT consolidation and/or maintenance • Early identification of lack/loss of response • Maintain or improve QOL • Salvage therapy when appropriate, considering disease and personal factors including advance care planning	
Survivorship	Health promotion and prevention		• Advance care planning • Continuation of survivorship planning • Discussion and support of end-of-life care when appropriate	

Note. MGUS = monoclonal gammopathy of uncertain significance; SMM = smoldering MM; NDMM = newly diagnosed MM; RRMM = relapsed and/or refractory MM; MM = multiple myeloma; MDE = myeloma-defining event; IMWG = International Myeloma Working Group; BMPC = bone marrow plasma cell; MRD = minimal residual disease; AHSCT = autologous hematopoietic stem cell transplant; QOL = quality of life. Information from Rajkumar et al. (2014).

sion, expected or unexpected treatment-related adverse events, and even periods of stable disease or remission, represent transition points that increase the vulnerability of the patient and their caregivers. If we consider the expanded continuum of care for MM (Figure 1), there are a number of key transition points that require specific attention. In addition, based on risk stratification, the tempo of the disease across the continuum of care may vary significantly. For example, a patient in a low-risk category such as asymptomatic MM may not require immediate disease-directed therapy but will benefit from early preventive and supportive care. Conversely, a patient with very-high-risk disease may derive limited benefit from the newest available therapies and experience a more aggressive disease trajectory. In many cases, the tempo of the disease may change unexpectedly or abruptly, emphasizing the need for early incorporation of advance care planning or escalation of palliative and supportive care. As with many chronic illnesses, treatment over an extended period of time, in most cases for life, raises important concerns about adherence to treatment recommendations and routines, and persistence in maintaining those routines. Given the inevitability

Table 2. Selected Clinical, Regulatory, Quality, and Reimbursement Measures With Implications for Multiple Myeloma Care

Regulatory/Quality initiatives	Key features/Recommendations	Clinical implications
Institute of Medicine 2005[a]	• All cancer survivors completing primary therapy should receive an SCP from their oncology provider that incorporates a written treatment summary and an individualized follow-up plan, including screening and prevention recommendations	• Any patient diagnosed with cancer is considered a cancer survivor • MM is considered a chronic condition in most cases, given improved survival • Adapting these recommendations to the MM population should facilitate communication among providers, improve health promotion, enhance prevention and surveillance activities, and improve QOL
American College of Surgeons Commission on Cancer	• Among other criteria, evidence of SCP implementation and patient navigation systems is required for COC accreditation	• Comprehensive care of the MM survivor should include: ○ Individualized care that is guided by standards of care, practice guidelines, and consensus statements ○ Coordinated care within the interdisciplinary team and among providers across practice settings ○ Empowerment of the patient and their caregivers to improve self-management
Affordable Care Act	• Expanded access to care, with a growing survivor population • Meaningful use mandating benchmarks for use of the EHR and patient-reported outcomes	• Incorporation of health promotion and disease prevention as a part of the MMCC, including smoking cessation, medication review, diet, and exercise • Use of the EHR to document patient care and track clinical outcomes • Inclusion of a patient portal to engage patients and their caregivers in their treatment decisions and monitoring
Institute of Medicine[b]	• Incorporation of shared decision making and personalized palliative and end-of life care for every patient living with cancer as a means to improve both the quality of care and cost efficiency[b] • ACP implemented early in the disease continuum	• Palliative and supportive care should be initiated for all patients diagnosed with MM, with adaptation as needed across the MMCC • ACP is addressed early in the diagnosis to include goals of care as well as patient wishes, including advanced directives and end-of-life care • ACP should be readdressed throughout the MMCC with particular attention to transition points, including cancer diagnosis and cancer progression, or when death is anticipated within a year[b]

Note. IOM = Institute of Medicine; SCP = survivorship care plan; MM = multiple myeloma; QOL = quality of life; COC = American College of Surgeons Commission on Cancer; EHR = electronic health record; MMCC = multiple myeloma continuum of care; ACP = advance care planning.
[a]Hewitt, M., Greenfield, S., & Stovall, S. (2005). Institute of Medicine report. From Cancer Patient to Cancer Survivor: Lost in Transition. Available at http://nap.edu/11468
[b]Institute of Medicine report. (2015). Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life. Available at http://nap.edu/18748

of relapse in the majority of MM cases, frequently changing the treatment routine introduces additional stressors. Vulnerable populations such as the frail patient, the very old, the younger patient, and those with limited caregiver support or socioeconomic strains require specific consideration to effectively balance disease response with QOL (Palumbo et al., 2015).

As a means to address the needs of patients over the entire continuum of care, the IOM has issued a series of reports establishing guidelines for survivorship care, palliative and supportive care,

psychosocial support, and end-of life care (Table 1; Nekhlyudov, Levit, Hurria, & Ganz, 2014). Key to these recommendations is improvement in QOL and active engagement of the patient in decision making about their care. Similarly, the National Comprehensive Cancer Network (NCCN) has published guidelines for palliative care and survivorship. The International Myeloma Working Group and the International Myeloma Foundation Nurse Leadership Board have published guidelines and consensus statements for supportive care specific to MM survivors (www.myeloma.org).

The focus of palliative care is to prevent suffering and improve QOL. Interdisciplinary symptom assessment and management focused on both the patient and the family at all ages and stages of life is at the core of palliative care (Levy et al., 2016). The World Health Organization (WHO) recommends that all patients with a life-threatening illness could benefit from palliative care (World Health Organization, 2002). The most recent NCCN guidelines suggest that palliative care should be initiated at the time of a cancer diagnosis, continue throughout the life of the cancer patient, and maintained concurrently with disease-directed therapy. Palliative care may become the primary method of care delivery in patients who are felt to no longer benefit from disease-directed therapy (NCCN, 2015). Palliative care services have been found to improve patient outcomes, reduce suffering, and prolong life (Meghani & Hinds, 2014).

Unfortunately, recent literature continues to suggest that QOL in MM survivors is lower than in any other hematologic malignancy and all solid tumors with the exception of pancreatic cancer (Kent et al., 2015). Kent and colleagues (2015) evaluated 16,095 cancer survivors, including 320 MM survivors. The MM patients in this study had a median age of 71 years, were predominately female (56.5%), and had been living with MM for an average of approximately 3 years (mean = 37.2 months). When comparing established measures of QOL, patients with MM rated their physical, social, emotional, and mental health lower than any other solid or hematologic malignancy patient group in this study, including those with pancreatic cancer (Kent et al., 2015). Interestingly, only those patients with pancreatic cancer or MM ranked their bodily pain significantly different than the 1,224,549 individuals without cancer used for comparison. Additional studies have identified continued unmet supportive care needs of both the MM patient and their caregivers. Molassiotis and colleagues (2011) evaluated 132 MM patients and 93 informal caregivers. The most commonly identified unresolved symptoms or concerns in the MM patients included anxiety (27.4%), depression (25.2%), tiredness (40.7%), pain (35.9%), insomnia (32.3%), peripheral neuropathy (28.3%), memory problems (22.3%), and concerns about the future (40.8%). Interestingly, almost half (48.8%) of the caregivers reported anxiety as an unmet need. Anxiety in both the patients and their caregivers was associated with higher perceived unmet needs. In qualitative analysis, concerns about the future reflected a sense of uncertainty. Anxiety about symptoms that might indicate recurrence or progression, "waiting for the other shoe to drop," and the late effects of the disease and treatment such as loss of height, cataracts, neuropathy, hearing loss, and graft-versus-host disease were among the concerns reported by patients (Molassiotis, Wilson, Blair, Howe, & Cavet, 2011). Engaging the patient and their caregivers in shared decision making has been found to reduce anxiety and improve QOL (Tariman et al., 2013).

Assimilating the rapidly evolving scientific advances and effectively integrating these into the care of patients living with MM presents a challenge for the advanced practice provider and the health care team. Effectively incorporating regulatory and quality measures and beginning to address the continued unmet needs of the patient and caregiver faced with the uncertain MM disease continuum present additional challenges. Although uncertainty remains, through continued clinical trials, collaborative practice, and consensus building among key opinion leaders, there is great hope for the future of MM patients. In an attempt to provide a summary of recent data and practice guidelines, and to provide insights gained from years of working with MM patients and their caregivers, the International Myeloma Foundation Nurse Leadership Board has compiled a series of articles with practical tools to assist the advanced practitioner in oncology in the clinical management and support of the MM patient.

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