Assessment of Knowledge and Performance Gaps in the Treatment of Patients with Multiple Myeloma

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Background: The literature on the treatment of patients with multiple myeloma (MM) has grown enormously in the past decade, especially with the introduction of novel therapies. Appropriately designed continuing medical education (CME) activities could help extend improvements in treatment outcomes to more patients, including those outside of academic medical centers.

Methods: An expert panel of CME professionals and clinicians treating MM was convened. Panel members contributed evidence regarding educational needs in MM. This evidence was discussed iteratively, and a schema was devised for designing educational interventions to meet those needs.

Results: Five high-priority educational goals were matched with desired outcomes. These goals included appropriate use of advanced testing methods, management of drug toxicities, individualized selection of treatment intensity, patient selection for stem cell transplantation, and use of maintenance or consolidation therapy. Approaches for developing CME activities to meet these needs were briefly outlined.

Conclusions: Advances in MM therapy promise improved survival and quality of life for many patients. In view of the enormous amount and complexity of the data to be mastered, CME is of paramount importance in achieving these benefits. Approaches for designing effective CME were outlined as a result of these meetings of clinical and education experts.

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29.9 months; $P < .001$), compared with patients who had received their diagnoses in the previous decade [2]. Some patients, however, have a poor prognosis because of the cytogenetic constitution of their malignant plasma cells. This subgroup of patients represents approximately 20% to 25% of all MM patients [3] and requires more effective and durable treatment options.

The large volume of research being conducted on MM has led to explosive growth in the literature. In addition to the publications appearing in a broad range of journals, more than 1000 abstracts of MM research are presented annually at meetings of the American Society of Hematology, the American Society of Clinical Oncology, the International Myeloma Workshop, and other societies. This large influx of new data presents challenges for community and academic oncologists who need to incorporate research findings into their practices in an evidence-based manner.

For the medical advances reported in these publications to provide the greatest possible benefit to patients, physicians need to be informed of the data, understand their implications, and develop strategies for implementing their application into practice. Optimal treatment requires understanding the complex genetics of MM disease biology and the clinical heterogeneity of the disease. The treatment methods selected must be effective against disease activity and must be as well-adapted as possible to patients’ needs, disease profiles, treatment preferences, and quality-of-life concerns. Physicians require educational exposure to novel treatments and their toxicities to appropriately incorporate these agents into their treatment decisions. In addition, community oncologists have the daunting task of staying current on more than 100 different types of malignancies. Finally, educational activities must support effective communication between healthcare providers, patients, and caregivers.

The decision was made to conduct a detailed analysis of the educational needs of healthcare providers treating patients with MM to help educators narrow some of the identified practice gaps. Clear identification of knowledge and performance gaps in the treatment of MM can help medical educators deliver effective evidence-based education to clinicians. Because several types of healthcare professionals with different learning needs and styles are involved with oncology care teams, a spectrum of educational activities will be needed to address these gaps.

### MATERIALS AND METHODS

#### Expert Panel Meetings

Two meetings of an expert panel of healthcare providers engaged in the management of MM (academic and community-based physicians and nurse practitioners), leaders of continuing-education organizations, and representatives of treatment coalitions and patient-advocacy groups were conducted to assess and prioritize educational needs for the treatment of MM (Figure). At the first meeting in October 2008, methods for collaboration and evidence-based approaches for identifying major educational gaps were discussed, data sources to be consulted were outlined, and important educational needs were discussed. The panel members were asked to define and document existing educational deficiencies. The resulting information was shared with all panel members by e-mail prior to the second meeting.

At the second expert panel meeting in February 2009, the participating clinicians were asked to comment on the current status of research in the treatment of MM, provide insights on the knowledge and attitudes of healthcare providers in regard to clinical implications of research findings, and validate the identified educational needs. The panel members used a nominal-group technique [4] to rank the significant barriers to optimal MM management by their importance, considering the perspectives of community and academic oncology practices. Identified educational gaps were discussed and categorized as knowledge or performance gaps. An iterative process that included dynamic interaction among the panel members permitted the delineation of educational needs that go beyond mere provision of data. This delineation extended into the members’ interpretation, application to practice, and communication about treatment choices with patients, their families, and other healthcare professionals.

#### Documentary Materials

Panel members contributed documentary sources of information (Table 1) during or before the second meeting of the expert panel. This information included data from the MM-treatment literature, requests for information made by physicians to education providers, comments and outcomes data from participants in continuing-education activities, and surveys conducted by education providers and the commercial supporter of this needs assessment, Celgene Corporation. The Celgene physician-survey data cited below provided valuable insight, not only on physicians’ practice patterns in varying treatment settings but also on specific gaps in knowledge and practice in this area of oncology.
Table 1. Summary of Documentary Information Sources Used in the Present Needs Assessment

- Medical literature
- Previous educational-activity evaluations and outcomes data
- Medical information queries
- Market or other research analyses
- Expert opinion
- Survey results
- Relevant guidelines and consensus documents

RESULTS: EDUCATIONAL NEEDS IDENTIFIED

After a preliminary review and discussion of the data provided by the panel members during the first meeting, the unmet educational needs were delineated and grouped under the main types of educational gaps that were identified. During the second meeting, the panel members further refined the knowledge and performance gaps and discussed related desired outcomes for educational activities (Table 2).

The clinicians and education providers agreed that one item initially identified as a separate educational need was actually a performance gap that affected all of the other needs: the difficulty of translating data from clinical trials into practice. It may be difficult for practicing oncologists to differentiate the implications of preliminary phase 2 clinical trials and the more comprehensive phase 3 clinical trials. Whereas current medical practice demands evidence-based treatment decisions, considerable time is required before published clinical trial data can be assessed and translated into comprehensive guidelines for patients in specific subgroups. In oncology, key study data are not included in drug product labels in a timely fashion because of the pace and complexity of developments in the field (eg, drug combinations).

This time discrepancy may represent a source of concern for patients and caregivers. Panel members noted that the MM patient community is a very proactive and well-educated group with strong global ties. Patients obtain information from independent reading and value the opportunity to discuss this information with their healthcare team.

Not only should oncologists feel confident about their therapeutic decisions, they also should have the resources necessary to reassure patients about their treatment, thereby supporting treatment adherence. Consideration of the long-term risks and benefits of various treatment approaches and discussion of these factors with patients to ascertain their preferences are key to achieving satisfaction with care.

The panelists identified and prioritized the following major areas (listed in decreasing order of importance below) for which current knowledge and performance regarding MM is inadequate. The identification and characterization of these areas therefore might suggest suitable desired learning outcomes for medical-education activities.

Methods (eg, Cytogenetics, Fluorescence In Situ Hybridization Testing) for Diagnosis, Classification, Risk Stratification, and Applying Results to Treatment Decisions

In February 2009, a Celgene-funded unpublished independent research study (N = 252) showed that although the majority of physicians surveyed routinely perform cytogenetic testing on MM patients, the test results are infrequently used as a basis for making treatment decisions. At first look, this discrepancy appeared to represent a knowledge gap regarding the usefulness of test results and a performance gap in applying the results; however, the discussion among the panel members suggested a different interpretation, a more subtle educational need than merely calling for additional data. Although there are data showing a benefit of some novel treatment options in MM patients with poor-risk cytogenetics, the data regarding the response to newer therapies as a function of cytogenetic analyses are often based on analyses of small subsets (eg, n = 30) and studies of inconsistent design. The clinicians agreed that the current status of knowledge is not adequate to mandate the use of cytogenetic results in making treatment decisions. It is important for physicians to be reassured that it is acceptable not to use cytogenetic test results in treatment planning because of the lack of sufficient evidence; however, it is critical that cytogenetic data be collected in clinical trials or registries, collated, and evaluated to enable their future use in tailoring therapies to specific diseases and patient needs.

Clinicians treating MM patients, especially clinicians based in the community rather than in academic medical centers, therefore would benefit from education regarding the cytogenetic abnormalities that occur in MM patients, the effects of these abnormalities on disease biology, and the implications of disease biology for treatment. Guides that support healthcare providers in discussing the subject of cytogenetic testing with patients might be useful.

Methods for Early Recognition of Toxocities and Appropriate Dosage Adjustment in the Case of Novel Agents

The adverse effects of novel therapies for MM are considerably different from those of older therapies (eg, alkylating agents) [5]. Strategies for anticipating and managing these adverse effects may not be widely known. The uncertainty about managing toxicities, such as peripheral neuropathy or deep vein thrombosis, might cause hesitation among patients and treating clinicians regarding the use of these novel agents. Oncologists and allied health professionals need to inform patients of the potential toxicities, be attuned to their tolerance of the drugs, and make the appropriate dosage adjustments when clinically indicated. Providers should have the information they need to reassure patients that it is feasible to carefully balance the benefits and risks of novel therapies with a variety of methods in order to mitigate side effects.

The potential for treatment side effects is a major reason why experts in MM
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<tr>
<th>Educational Needs</th>
<th>Reasons for Gaps</th>
<th>Desired Outcomes</th>
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<tbody>
<tr>
<td>Applies to all other needs:†</td>
<td></td>
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<tr>
<td>• Translating presented or published data from clinical trials into practice</td>
<td>Knowledge gap&lt;br&gt; • Volume of new data is enormous; data are complex</td>
<td>Continually update knowledge</td>
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<td></td>
<td>Performance gap&lt;br&gt; • High-level synthesis is required to incorporate new information into clinical practice</td>
<td>Effectively integrate emerging data into patients’ treatment plans</td>
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<tr>
<td>• Appropriate use of methods (eg, cytogenetics, FISH testing) for diagnosis, classification, risk stratification of MM, and appropriate application of results to treatment decisions</td>
<td>Knowledge/attitude gap&lt;br&gt; • Insufficient data are currently available to indicate utility of cytogenetic/FISH results for guiding treatment (some physicians and patients think cytogenetic data should have clinical utility, but they need to understand that it is not yet possible to use these data to guide treatment)</td>
<td>Explain the potential biologic rationale for cytogenetic and FISH testing&lt;br&gt; Cite the implications of the current lack of data on utility of cytogenetic test results for treatment decisions and need for data accumulation</td>
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<td>Performance gap&lt;br&gt; • Tests are not always ordered, and results are not always collected and documented for future use</td>
<td>Order appropriate tests, collect data, and document results&lt;br&gt; Effectively integrate emerging data on cytogenetic testing into patients’ treatment plans</td>
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<td>• Early recognition of toxicities and appropriate dosage adjustment to manage them</td>
<td>Knowledge gaps&lt;br&gt; • Possible toxic effects of novel agents are not well known&lt;br&gt; • Ways to mitigate toxicities, including acceptable dosage adjustment or alternative methods, are not widely discussed</td>
<td>Identify potential toxicities of novel therapies&lt;br&gt; Describe methods to mitigate anticipated toxicities</td>
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<td>Performance gaps&lt;br&gt; • Physicians and allied health professionals (&quot;providers&quot;) need to effectively discuss possible treatment toxicities with patients and question them about symptoms and signs of toxicities&lt;br&gt; • Providers should reassure patients that toxicities can be managed without disrupting their cancer treatment</td>
<td>Discuss treatment toxicities with patients and facilitate patients’ early identification of adverse events&lt;br&gt; Recognize early signs of toxicities characteristic of novel therapies&lt;br&gt; Manage toxicities effectively&lt;br&gt; Effectively integrate emerging data on toxicity management into patients’ treatment plans</td>
</tr>
<tr>
<td>• Comparing implications of achieving CR versus VGPR for treatment decisions</td>
<td>Knowledge gap&lt;br&gt; • Weigh available treatment-response criteria and their implications for overall survival and patient quality of life</td>
<td>Catalog type, depth, and duration of response attainable with different treatments</td>
</tr>
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<td>Performance gap&lt;br&gt; • Elicit and discuss preferences of patients and families/caregivers for quality of life and overall survival</td>
<td>Effectively discuss options with patients and outline trade-offs between responses and treatment side effects&lt;br&gt; Effectively integrate emerging data on response criteria into patients’ treatment plans</td>
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<tr>
<td></td>
<td>Attitude gap&lt;br&gt; • Clinicians often do not respect patient preferences</td>
<td>Demonstrate empathy and respect</td>
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management [6] point out the need to weigh the potential benefits of aggressive treatment of MM against the adverse effects of such treatment and the quality-of-life impairments they may cause. Some patients would prefer to undergo treatments that promise a greater depth and duration of remission at the potential expense of increased toxicities. In contrast, other patients are unwilling to jeopardize their quality of life to achieve a deeper and more durable remission. The need for good communication among patients, their families, and the full spectrum of healthcare providers involved in their care is especially acute in this area.

### Importance of Targeting Depth of Response in Treatment Decisions

Healthcare providers who attended educational activities developed by several of the education partners on the panel requested additional information on the depth of response that should be targeted. Oncologists participating in the expert panel meeting noted that the advantages of targeting a very good partial response (90% improvement in myeloma paraprotein) are becoming more widely recognized, but many questions remain to be answered about the desirable depth of response—for example, a complete response (CR) or a stringent CR—at various stages of treatment. This question highlights a knowledge gap, in that some community oncologists may not be aware of the advantages of targeting a very good partial response [6].

Currently, MM is not considered curable today: Minimal residual disease remains in all patients following therapy (excluding the small group of patients selected to undergo allogeneic [donor] transplantation), and patients eventually die from disease relapse. Ultimately, because long-term survival is now the norm, most patients will eventually be exposed to all agents over the course of their treatment. Therefore, controlling disease to prevent relapse is the most relevant goal of therapy. The time to disease progression is the parameter most closely correlated with overall survival; prolonging overall survival is considered the ultimate goal of therapy by both academic and community physicians.

### Current Place of Autologous Stem Cell Transplantation in MM Therapy

The availability of new induction-chemotherapy regimens for MM patients has begun to alter physicians’ opinions about the use of autologous stem cell transplantation (SCT) as a definitive part of first-line management. If induction chemotherapy leads to CR or a near CR, many physicians treating MM patients now consider the use of SCT for intensification or consolidation of the response. In an independent market

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**Table 2 (CONT.)**

<table>
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<th>Educational Needs</th>
<th>Reasons for Gaps</th>
<th>Desired Outcomes</th>
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| Safe and effective use of SCT (who, when, and how many times?) | Knowledge gap  
- Few data are available comparing outcomes of different SCT policies in the era of novel therapies; existing published research was done with older therapies | Continually update knowledge on appropriate use of SCT |
| Safe and effective use of maintenance therapy after initial response to cytotoxic therapy or SCT (who, when, what treatment, and for how long?) | Knowledge gap 
- Insufficient data are available to indicate pros and cons of various maintenance (or consolidation) therapy options after treatment with novel agents; current data pertain only to older therapies | Continually update knowledge on maintenance therapy with novel agents |

“FISH indicates fluorescence in situ hybridization; MM, multiple myeloma; CR, complete response; VGPR, very good partial response; SCT, stem cell transplantation.

†This row applies to all other needs.
research survey (N = 271) conducted by Celgene in September 2008 (unpublished), when oncologists were asked, “How has the availability of new induction regimens for myeloma changed your use of autologous transplant as part of definitive first-line management?” approximately 40% stated that they plan to perform SCT to improve or extend the good results achieved with the induction regimen, whereas approximately 40% chose to defer SCT and approximately 12% said they would stop treatment and observe the patient. In addition, approximately 40% of the queried oncologists stated that they were now more likely to base their recommendation for SCT on the patient’s response to induction therapy; 27% said they were less likely to recommend transplantation than they were in the past. No change in opinion was reported by 26% of the respondents, but 7% stated that they were more likely than they were in the past to recommend SCT. Most of these physicians recommended continued chemotherapy at some level for some interval. Approximately 20% of the physicians surveyed said they refer to the transplantation physician to make this decision. Community-based oncologists have a less clear conviction for transplantation than academic oncologists (38% versus 50%, respectively).

As a modality, SCT has been shown to be superior to older, conventional therapies [7,8]; however, SCT has not been directly compared with the novel agents currently available. Therefore, the available data are not fully adequate to answer the myriad questions about SCT in the era of novel therapies, and trials are being planned to compare novel therapies with SCT. In the interim, physicians need to reassure patients that there is no single correct answer to this question and that they will be treated according to the best available knowledge, as well as their own preferences. In addition, whenever possible, patients should be referred to participate in clinical trials.

Maintenance Therapy after Initial Chemotherapy Response or SCT
Maintenance therapy is an additional topic around which circumstances have changed with the introduction of novel agents, and data to support treatment choices are still being analyzed. New phase 3 data, which were expected to be presented in this area at the American Society of Hematology meeting in 2009, will provide some data to assist in this decision.

ADDRESSING IDENTIFIED EDUCATIONAL NEEDS
These identified knowledge and performance gaps should be the basis for the development of educational activities that effectively address physicians’ needs. The last column in Table 2 presents examples of desired outcomes for educational activities designed to narrow these gaps. The identified needs are being shared with the oncology and continuing-education provider communities to help educators develop appropriate and effective interventions for narrowing these gaps. The activities should be modeled on the latest information about effective physician education, as is briefly outlined below.

A comprehensive report published in February 2007 by the Agency for Healthcare Research and Quality systematically reviewed the literature to determine the effectiveness of CME [9]. According to this report, such CME activities as case-based learning, live programs, and printed materials have positive short- and long-term effects on practice behavior objectives and are “effective at the acquisition and retention of knowledge, attitudes, skills, behaviors, and clinical outcomes.” The adult-learning literature indicates that effective CME is associated with at least 4 factors [10-14]:

1. Needs assessment and a focus on higher-level outcomes. For example, activities may be planned on the basis of needs-assessment data gathered from initiatives such as the expert panel meetings described in this document and the background materials supplied by the participants—survey, information-request, and literature data—which demonstrated gaps in knowledge and performance on medical issues surrounding MM.

2. Planning that pays attention to the context in which the learned principles will be applied. Content for activities should be developed by practitioners who are sensitive to the settings in which this knowledge will be used and the target audience.

3. Interactive learning. Professional practice can change significantly when learning is made more interactive through case presentations.

4. Integration into practice. Practitioners should be encouraged to take information back to their practice settings and apply it to the delivery of medical care to patients. Time-efficient access to educational content is also necessary for it to be used in patient care.

Proposed activities should be designed to facilitate the 3 stages of the “predisposing-enabling-reinforcing” model of learning described by Davis and colleagues [15,16]. Reinforcing activities are particularly effective in bringing about long-term practice changes; therefore, series of sequenced activities with follow-up to consolidate learning are advisable. It is hoped that the knowledge acquired from these activities will lead to behavior change in the clinical setting, once participants are given the opportunity to practice what they have learned.

Although certified CME is supposed to be evidence based, much of oncology practice faces an additional set of challenges in meeting the educational standards set for other diseases. This is due to the urgency of communicating lifesaving developments and the importance of making the best-possible treatments available to patients at the earliest time consistent with the strongest possible evidence of effectiveness and safety. It will remain a challenge
for continuing-education providers accredited by the Accreditation Council for Continuing Medical Education to provide “evidence-based content” in light of the rapidly evolving literature base and the lag time for updating guidelines and consensus statements in oncology, particularly for less common malignancies such as MM.

**BEYOND STANDARD CME**

Panelists reported that MM patients are very interested in pursuing knowledge about their prognosis and available treatments and frequently consult Web sites available through the International Myeloma Foundation, the Multiple Myeloma Research Foundation, and the Leukemia and Lymphoma Society. Healthcare providers and patients could benefit from more extensive awareness of available patient-education materials, including educational/informational materials to increase patients’ understanding of therapies and their potential toxicities. Many of these materials are available at no cost online or through direct mailing from the aforementioned resources. Patients may value support from oncologists and allied health professionals in locating and using these materials, and therefore it is important that these professionals be aware of the available materials.

In view of the paramount importance of clear communication in all healthcare-related interactions, oncologists and other providers could benefit from interventions or aids that help them explain to patients, their families, and primary care physicians the therapeutic choices to be made and their consequences for survival and the quality of life. Educating patients about symptoms of drug toxicities can help to ensure that patients report any signs of these adverse events in time to help prevent the most severe consequences. A variety of interventions and tools for patients, general practitioners, and allied health professionals are available and could be adapted to support patient and physician education about drug toxicities. Patients’ understanding of the benefits and potential drawbacks of available therapeutic options is also very important for promoting treatment adherence.

**CONCLUSIONS**

The novel therapies for MM treatment that have been introduced in the past decade are enhancing patients’ survival and quality of life. The explosion of data regarding MM treatments requires up-to-date educational activities to inform clinicians about the multitude of effective treatment options. Such activities are especially crucial because of the time lag from the presentation of clinical trial results in the form of meeting abstracts until the publication of complete reports in peer-reviewed journals and the incorporation of the results into treatment recommendations and guidelines.

Collaboration between physicians specializing in the treatment of MM patients and medical-education specialists is necessary to facilitate the sharing of knowledge and methods for practice improvement. The inclusion of allied health personnel and representatives of patient-advocacy groups in the body making educational recommendations will help ensure that patients’ clinical and psychosocial needs are considered. Communication between providers and patients is a critical issue, especially for diseases such as MM for which therapies are changing rapidly. Facilitating such communication should be a goal included in many educational activities.

The study we have described indicates that knowledge and performance gaps overlap rather than represent discrete needs and should be addressed systematically in educational activities tailored to different categories of healthcare providers. Such activities must be updated frequently, in view of the very rapid pace of scientific progress and publication in this area. Furthermore, in the case of this uncommon disease, it is important that the educational resources be readily available through a variety of formats for use when needed, because the time from the provider’s completion of an educational activity to the time when the next MM patient is seen may be relatively long.

A body of educational research is available to guide the development of effective CME. Applying these data to the identified gaps in the treatment of MM patients may optimize educational effectiveness. Designing educational interventions to achieve the desired outcomes we have outlined may be a fruitful route to performance improvement.

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