Tolerance and Response to Initial Systemic Therapy in Younger and Older Patients with Multiple Myeloma: A Cross-Sectional Case Survey with 276 Unselected Recent Cases in the Practices of US-Based Medical Oncologists

#1516

N Love, MD[1]; S Lonial, MD[2]; K Anderson, MD[3]; R Fonseca, MD[4]; K Ziel, PhD[1]; M Elder, BBA[1]; D Paley, BA[1]; A Asnis-Alibozek, MPAS, PA-C[1]

[1] Research To Practice, Miami, FL; [2] Emory University Winship Cancer Institute, Atlanta, GA; [3] Dana-Farber Cancer Institute, Boston, MA; [4] Mayo Clinic Cancer Center, Scottsdale, AZ

BACKGROUND:

Multiple myeloma (MM) is generally considered incurable, but the rapid integration of IMiDs® and proteasome inhibitors into systemic anticancer treatment has resulted in clinically important improvements in response rates, disease control and overall survival. A number of factors influence selection of initial systemic therapy, particularly patient age and whether autologous stem cell transplant is planned. A paucity of information exists on how often clinicians are called upon to make these primary treatment decisions, which specific regimens are selected for patients in different age groups and the resultant outcomes. In order to assess the education gaps in this field, clinical information on individual patients receiving initial treatment for MM was gathered and examined.

METHODS:

US community-based medical oncologists were recruited from a database of past participants in Research To Practice CME activities to participate in a cross-sectional case survey by providing anonymous information on presenting symptoms, diagnostic workup, treatment selection, side effects and clinical antitumor response for all patients in their practices with a new diagnosis of active MM since January 1, 2008. Modest, per-patient honoraria were provided for this work.

These oncologists were also asked to complete a 60-question Patterns of Care survey designed to assess their recent MM decision-making experiences and also to define their self-described treatment recommendations for a number of related hypothetical clinical scenarios.

RESULTS:

Frequency of MM-Related Treatment Decisions

Responses provided during the Patterns of Care survey indicate that participating oncologists address a variety of common MM-related treatment decisions during a typical year.

Decisions regarding induction treatment for patients not eligible for transplant are addressed on average every 10 weeks and for patients eligible for transplant, every three months (Figure 1).

General Case Information and Patient Demographics

From April 14 to July 9, 2010, a total of 276 cases of MM were entered into a web-based data collection instrument by 43 US-based medical oncologists. A median of six cases per participant were recorded, with a minimum of one and a maximum of 14 (Figure 2).

Demographics:

- Median patient age was 68, with 34 percent younger than age 65, 36 percent age 65 to 74 and 30 percent age 75 years or older.
- Fifty-four percent of the patients were men.

1 APPROXIMATELY HOW OFTEN PER YEAR DO YOU MAKE THE FOLLOWING DECISIONS RELATED TO MULTIPLE MYELOMA?*

	Median
Induction therapy, transplant eligible	4
Maintenance therapy, received transplant	2
Induction therapy, not transplant eligible	5
Maintenance therapy, has not received transplant	4
Use of bone-targeted treatment	8

* Patterns of Care survey of 45 medical oncologists recruited for the cross-sectional case survey

2 CROSS-SECTIONAL CASE SURVEY OF 276 UNSELECTED CONSECUTIVE PATIENTS RECEIVING INITIAL THERAPY FOR MULTIPLE MYELOMA

- 43 community-based oncologists representing 14 states who participated in prior CME activities
- All cases diagnosed and treated since January 2008
- Expansion of previous case-data collection initiative implemented in 2009
- Database open from April through July 2010
- Individual MM case data collected:
  - Median number of cases: 6
  - Maximum cases submitted by one physician: 14

3 HOW SYMPTOMATIC (DISEASE RELATED) WAS THIS PATIENT AT THE TIME TREATMENT WAS INITIATED?

	Overall (n = 276)	<65 yo (n = 95)	65-74 yo (n = 98)	≥75 yo (n = 83)
Very symptomatic	30%	33%	28%	28%
Moderately symptomatic	37%	34%	37%	42%
Mildly symptomatic	26%	25%	30%	24%
Not at all symptomatic	7%	8%	5%	6%

4 WHAT WAS THE PATIENT'S RISK PROFILE BASED ON METAPHASE CYTOGENETICS AND/OR FISH ANALYSIS?

	Overall (n = 276)	<65 yo (n = 95)	65-74 yo (n = 98)	≥75 yo (n = 83)
Standard risk	64%	66%	61%	66%
Poor risk	24%	27%	29%	15%
Not evaluated	12%	7%	10%	19%

Symptomatology:

Overall, more than two thirds of patients were considered to be very symptomatic or moderately symptomatic from the disease at the time treatment was initiated (Figure 3). The fraction of patients experiencing varied levels of symptomatology was similar across the three age groups (Figure 3).

Molecular Diagnostics:

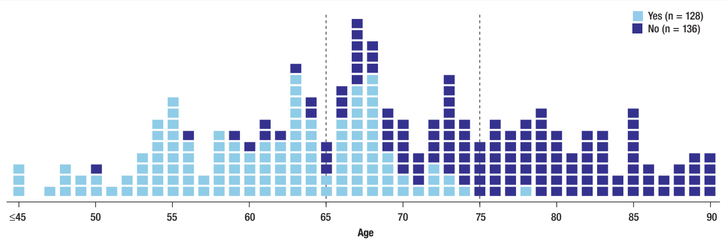
Eighty-eight percent of patients had their tumors evaluated by metaphase cytogenetics and/or FISH. Overall, two thirds of the patients were considered to be at "standard risk," with no remarkable differences across the three age groups (Figure 4).

Transplant Eligibility

Approximately half of the patients were deemed eligible for stem cell transplant (SCT) by their treating physician (Figure 5). Patients younger than age 70 were much more likely to be considered for SCT, as would be expected.

- Median age of transplant-eligible patients: 62 years
- Median age of transplant-ineligible patients: 76.5 years
- Age of oldest patient considered for SCT: 78 years
- Age of youngest patient deemed unsuitable for SCT: 50 years

5 DID YOU INITIALLY CONSIDER THIS PATIENT TO BE A CANDIDATE FOR STEM CELL TRANSPLANT? (N = 264 ASSESSED)



6 CHOICE OF INDUCTION REGIMENS

Most common induction regimens:

Transplant eligible (n = 128)		Transplant ineligible (n = 136)	
Rd/RD	29%	VD	21%
RVD	26%	Rd/RD	20%
VD	23%	MPT	16%
		MPV	16%

Induction Regimens

Transplant-eligible patients most frequently received lenalidomide- or bortezomib-based doublet regimens or the lenalidomide/bortezomib/dexamethasone (RVD) triplet (Figure 6).

Induction therapy for transplant-ineligible patients included doublets containing an IMiD and bortezomib alone or with melphalan (Figure 6).

Treatment Response and Safety/Tolerability

Overall, 86 percent of patients were reported as having at least a partial response as assessed by their treating oncologist. The majority of patients tolerated treatment well with only 18 percent experiencing clinically significant or major side effects (Figure 7).

No substantial differences in short-term response rates and tolerability to treatment were found across the patient age groups (Figure 7).

Clinician-reported response to therapy among patients receiving the five most frequently selected treatment regimens varied only slightly. However, a higher percent of complete responses was documented for patients receiving RVD compared to those treated with other induction therapies (Figure 8).

The percent of patients experiencing only mild to moderate side effects did not appear to differ substantially by therapy received (Figure 8).

Differences in specific side effects reported for each treatment group include higher reporting of peripheral neuropathy for the bortezomib-containing regimens (MPV, VD, RVD), greater incidence of neutropenia in the melphalan groups (MPT, MPV) and a slightly lower overall reported incidence of nausea/vomiting, fatigue and peripheral neuropathy with Rd/RD, relative to other major treatment groups.

7 CLINICIAN-REPORTED RESPONSES TO AND TOLERABILITY OF INITIAL INDUCTION REGIMENS OVERALL*

Response to treatment	Overall (n = 237)	<65 yo (n = 83)	65-74 yo (n = 85)	≥75 yo (n = 69)
Complete response	22%	24%	28%	13%
Partial response	64%	62%	59%	72%
Minimal response/stable disease	8%	7%	7%	12%
Progressive disease	6%	7%	6%	3%
Overall side effects and toxicities	(n = 269)	(n = 94)	(n = 98)	(n = 77)
Therapy went very well: Same or fewer problems than expected	38%	40%	37%	36%
Therapy went fairly well: Minor or moderate problems, not difficult to manage	44%	49%	41%	42%
Significant problems that were difficult to manage	15%	8%	20%	18%
Major problems with significant consequences	3%	3%	2%	4%

* Excludes patients not receiving treatment or in early treatment and not yet evaluated

8 CLINICIAN-REPORTED RESPONSES TO AND TOLERABILITY AND SAFETY OF FIVE MOST COMMONLY SELECTED INITIAL INDUCTION REGIMENS*

Response to treatment	Rd/RD (n = 59)	VD (n = 53)	RVD (n = 30)	MPT (n = 22)	MPV (n = 21)
Complete response	22%	17%	50%	14%	5%
Partial response	66%	68%	40%	68%	90%
Minimal response/stable disease	9%	9%	3%	14%	5%
Progressive disease	3%	6%	7%	4%	0%
Overall side effects and toxicities	(n = 65)	(n = 63)	(n = 36)	(n = 26)	(n = 22)
Therapy went/is going very well: Same or fewer problems than expected	45%	43%	39%	35%	9%
Therapy went/is going fairly well: Minor or moderate problems, not difficult to manage	46%	33%	47%	38%	73%
Significant problems that were/are difficult to manage	9%	21%	8%	23%	18%
Major problems with significant consequences	0%	3%	6%	4%	0%
Clinically relevant side effects†	(n = 65)	(n = 63)	(n = 36)	(n = 26)	(n = 22)
Fatigue	45%	62%	56%	62%	73%
Peripheral neuropathy	11%	48%	44%	19%	95%
Thrombocytopenia	31%	40%	31%	38%	64%
Neutropenia	31%	29%	25%	50%	55%
Myalgia/muscle cramps	15%	13%	22%	15%	23%
Nausea/vomiting	5%	17%	14%	19%	18%
Venous thromboembolism	5%	5%	17%	12%	9%

* Excludes patients not receiving treatment or in early treatment and not yet evaluated; † May include more than one response per regimen
R = lenalidomide; d = dexamethasone (low dose); D = dexamethasone (high dose); V = bortezomib; M = melphalan; P = prednisone; T = thalidomide

CONCLUSIONS:

Use of an online cross-sectional case survey enabled the collection of a significant amount of information on unselected MM cases during a three-month time period. Analysis of these data indicates the following:

- Benefits and side effects do not appear to vary significantly across the three selected age groups, suggesting that practicing oncologists are able to modify treatment selection, dose and schedule to achieve similar results for both older and younger populations without a disproportionate difference in toxicity.
- The induction therapies reported by practicing oncologists in this cross-sectional case survey tend to follow published guidelines regarding the use of RD/Rd, VD and RVD for transplant-eligible patients and RD/Rd, MPV and MPT for transplant-ineligible patients.
- The response and side effects/toxicity data from this cross-sectional case survey are consistent with the findings from previously published clinical trial data.

Although additional work is merited to further understand and compare specific doses and schedules of the treatments administered as induction therapy for MM, these survey findings suggest that the rapidly developing clinical research in this area is being effectively applied by medical oncologists to the care of their patients.

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