Implications of rapidity of response to initial therapy in multiple myeloma

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Background

- Survival in multiple myeloma has significantly improved over the past decade with introduction of new management strategies.
- The rapidity of response to initial therapy in multiple myeloma (MM) depends on a variety of factors such as the type of therapy, the disease biology, and the parameters of disease measurement.

Objectives

- There is limited data on the longer term implications of the rapidity of response following initial therapy in newly diagnosed MM patients (pts).
- This study was conducted to guide in the development of prospective clinical trials that would evaluate a response adapted therapy strategy and better understanding disease biology in MM.

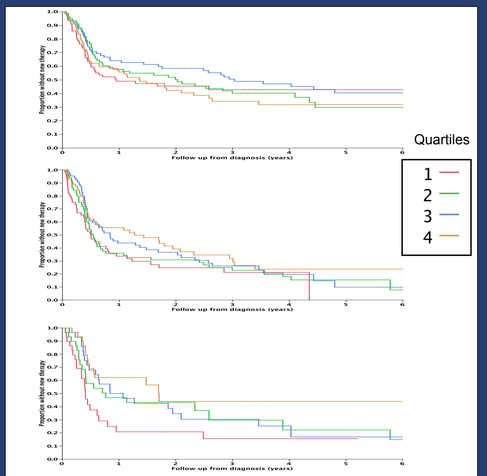
Conflict of interest: nothing to disclose

Methods

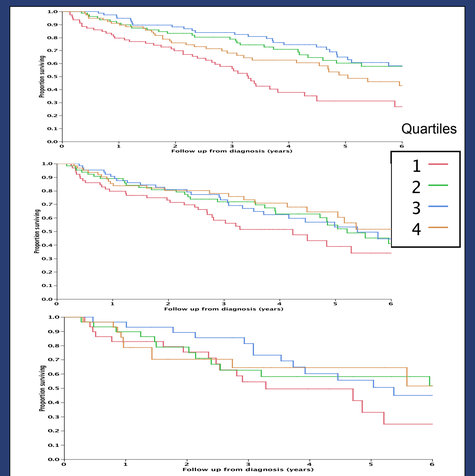
- A cohort of newly diagnosed MM patients treated with various regimens were identified from medical record. These patients were diagnosed between Jan 2000- Dec 2011 and seen at our institution for their initial evaluation and treatment.
- We collected serum M spike, urine M spike and free light chains data available after first cycle, second cycle and 4th cycle of chemotherapy, as well as other clinical and laboratory data.
- We identified the best response achieved according to IMWG response criteria.
- Patients who were previously treated and do not have any baseline and follow up laboratory values after 1st and 2nd cycle of chemotherapy were excluded from the study.
- Patients were divided into quartiles based on % reduction in serum M spike, dFLC, or urine M protein. JMP version 10.0 software was used for statistical analysis.

Results

- Total No of pts: 454, 62% male, 54% alive at last follow-up. Median follow up time was 4.9 yrs (95% CI; 4.4-5.5); and median overall survival (OS) was 5.4 yrs (95% CI; 4.8-6.5).
- Patients had measurable disease as defined by serum M-spike (>= 1 g/dL), dFLC (>=10 mg/dl) or 24- hour urinary M protein excretion (>=200 mg) in 70%, 72% and 42% respectively.
- There was no significant difference in the time to next therapy based on the early response after cycle 1.
- Median OS was poorest for patients with the least reduction of serum M protein (3.3 years) and for those with the most reduction in serum M-spike (5.1 years); P<0.001
- In a multivariate analysis, quartile 1 and 4 of serum M-protein response and the high-risk FISH were independent risk factors associated inferior OS.



Time to start of 2nd therapy for Serum M-protein (top), dFLC (middle) and Urine M-protein(bottom) decrease in quartiles.



Overall survival for Serum M-protein (top), dFLC (middle) and Urine M protein(bottom) decrease in quartiles.

Relationship between outcome and response to rapidity in cycle 1

Quartile	Upper limit % decrease	≥PR (%)	≥VGPR (%)	TTNT (years)	OS (years)
Serum M-protein (Median)					
1	25 (12.5)	44	5	1.0	3.3
2	46 (37)	75	24	2.0	7.6
3	63 (53)	89	38	3.0	7.4
4	100 (77)	97	74	1.4	5.1
p		< 0.01	< 0.01	NS	< 0.01
Serum FLC (Median)					
1	40 (6)	46	12	0.5	4.2
2	69 (55)	70	29	0.6	5.2
3	87 (80)	93	43	0.9	5.4
4	100 (96)	95	83	1.3	6.7
p		< 0.01	< 0.01	NS	NS
24-hour urine M-protein (Median)					
1	41 (7.4)	41	26	0.4	3.3
2	75 (66)	54	33	0.8	6.2
3	99 (93)	96	54	1.0	5.4
4	100 (100)	92	80	1.7	7.4
p		< 0.01	< 0.01	NS	NS

Conclusions

- Both shallow and very deep response to therapy in cycle 1 is a strong indicator of eventual disease outcome and should be considered as marker of high-risk disease.
- For the shallow responders, prospective trials should assess if a change in therapeutic management early after initiation of initial therapy will alter the outcome of these patients.
- The rapid deep responders also appear represent a different high-risk biology, emphasizing the fact that patients with high-risk disease often have excellent initial responses, but poor long term outcomes.