INTERVIEW

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Tracks 1-10

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: How do you approach the choice of induction regimen for patients with multiple myeloma (MM) who are eligible for transplant?

PROF CAVO: Transplant-eligible patients should receive an induction regimen containing at least one novel agent. We divide the induction regimens into those that are bortezomib based, those that are IMiD® based and a third class that includes both bortezomib and an IMiD. A three-drug regimen is clearly superior to a two-drug regimen in terms of a higher rate of complete response or very good partial response before autotransplant, and these responses are further improved after the autologous stem cell transplant. I believe that the best induction regimen for a younger transplant-eligible patient is probably a three-drug regimen incorporating both bortezomib and an IMiD, such as

lenalidomide. Such a combination seems to offer the highest complete response rate before transplant (Richardson 2010; [4.1]).

4.1

Prospective Phase I/II Study of Bortezomib, Lenalidomide and Dexamethasone (RVD) in Newly Diagnosed Multiple Myeloma

	All patients (n = 66)	Phase II patients (n = 35)
Complete response (CR)/near-CR	40%	57%
Very good partial response or better	67%	74%
Partial response or better	100%	100%

"This phase 1/2 study, the first prospective investigation of the regimen of lenalidomide-bortezomib-dexamethasone in newly diagnosed MM, has shown the combination to have favorable tolerability during a lengthy period, with no treatment-related mortality. This regimen is the first of its kind to result in a 100% response rate."

Richardson PG et al. *Blood* 2010;116(5):679–86.

Track 3

DR LOVE: What are your thoughts on induction therapy for older patients or those who are ineligible for transplant?

PROF CAVO: For patients with myeloma who are transplant ineligible, the standard combinations so far include melphalan/prednisone/thalidomide (MPT) and melphalan/prednisone/bortezomib (MPV). At ASH 2009 results were presented of a Phase III three-arm study evaluating standard MP, MP combined with lenalidomide (MPR) and MPR followed by maintenance lenalidomide (Palumbo 2009; [4.2]). The results reported that MPR followed by maintenance lenalidomide improves the clinical outcome significantly in comparison to standard MP. This provides us with a third combination for transplant-ineligible myeloma and demonstrates the role of maintenance lenalidomide for such patients.

Tracks 4, 10

DR LOVE: Where are we in terms of the schedule of bortezomib in the management of MM?

PROF CAVO: In my view, the most important issue in the nontransplant setting regarding the use of bortezomib is the recognition that changing from a twice-weekly schedule to a once-weekly schedule does not reduce the efficacy but significantly lowers the incidence of neurological toxicity (Bringhen 2010; [4.3]). It is also important to explain clearly to patients the symptoms of neuropathy and to advise them that at the first onset of one of the symptoms they should call the doctor and ask for a consultation. Physicians

will then be able to appropriately reduce the bortezomib dose or even stop the treatment in cases of neurological toxicity. Bortezomib dose modification is mandatory for achieving resolution or a decrease in the grade of neurological toxicity. ■

4.2

Response Rates and Progression-Free Survival (PFS) in a Phase III Study Evaluating MP versus MPR versus MPR-R for Elderly Patients with Multiple Myeloma

Efficacy	MPR-R (n = 152)	MPR (n = 153)	MP (n = 154)	*p*-value (MPR-R vs MP)
Overall response rate[1]	77%	67%	49%	<0.001
CR rate[2]	18%	13%	5%	<0.001
≥VGPR rate[3]	32%	33%	11%	<0.001
PR rate	45%	34%	37%	—
Median PFS	Not reached	13.2 months	13.0 months	<0.001

[1] As measured using EBMT criteria (Blade 1998); [2] Immunofixation-negative with or without bone marrow confirmation; [3] VGPR: >90% reduction in M-protein
M = melphalan; P = prednisone; R = lenalidomide; CR = complete response; VGPR = very good partial response; PR = partial response

Palumbo A et al. *Proc ASH* 2009;**Abstract 613**; Blade J et al. *Br J Haematol* 1998;102(5):1115-23.

4.3

Efficacy and Peripheral Neuropathy (PN) with Once-Weekly versus Twice-Weekly Bortezomib for Elderly Patients with Newly Diagnosed Multiple Myeloma

	Weekly bortezomib regimen (n = 372)	Twice-weekly bortezomib regimen (n = 139)
Median progression-free survival	33.1 months	31.7 months
Three-year survival	88%	89%
Overall response	85%	86%
Complete response	30%	35%
PN at 18 months (all grades)	40%	72%
PN at 18 months (Grade 3 or 4)	9%	36%

Bringhen S et al. *Blood* 2010;116(23):4745-53.

SELECT PUBLICATIONS

Bringhen S et al. **Efficacy and safety of once weekly bortezomib in multiple myeloma patients.** *Blood* 2010;116(23):4745-53.

Palumbo A et al. **A Phase III study to determine the efficacy and safety of lenalidomide in combination with melphalan and prednisone (MPR) in elderly patients with newly diagnosed multiple myeloma.** *Proc ASH* 2009;**Abstract 613**.

Richardson PG et al. **Lenalidomide, bortezomib, and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma.** *Blood* 2010;116(5):679-86.