INTERVIEW

Ruben Niesvizky, MD

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Tracks 1-11

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: Would you discuss the work you recently presented at ASH on the UPFRONT study in newly diagnosed multiple myeloma?

DR NIESVIZKY: UPFRONT is a randomized Phase IIIb study for patients who are not eligible for stem cell transplant, and therefore patients older than age 65 are significantly represented. The goal is to evaluate a bortezomib-containing induction regimen — bortezomib/melphalan/prednisone (VMP), bortezomib/thalidomide/dexamethasone (VTD) or bortezomib/dexamethasone (VD) — followed by a bortezomib-containing maintenance regimen. This is the first time such an approach is being used for elderly patients.

Peripheral neuropathy was common, with the lowest rates on the VD arm and the highest rates on the VTD arm. Overall, the responses were higher on the VTD arm when compared to VMP or VD, although the difference was not

statistically significant (Niesvizky 2010; [4.1]). An interesting observation is that the group of patients receiving VD is performing as well as the other groups. It is possible, at least in this elderly population, that we can administer two agents and still maintain the same efficacy with perhaps even less toxicity.

4.1

UPFRONT Study: Bortezomib-Based Induction (I) Followed by Weekly Bortezomib Maintenance (M) for Elderly Patients with Newly Diagnosed Multiple Myeloma

	VD (n = 167)		VTD (n = 168)		VMP (n = 167)	
Efficacy endpoints*						
Median PFS	13.8 mo		18.4 mo		17.3 mo	
	I	**I + M**	**I**	**I + M**	**I**	**I + M**
ORR	68%	71%	78%	79%	71%	73%
CR + nCR	24%	31%	36%	38%	31%	34%
Peripheral neuropathy (PN)						
Grade ≥3 PN	15%	5%	26%	6%	20%	2%
Grade ≥3 PN resulting in discontinuation of all study drugs	4%	4%	13%	0%	14%	0%

V = bortezomib; D = dexamethasone; T = thalidomide; M = melphalan; P = prednisone; PFS = progression-free survival; ORR = overall response rate; CR = complete response; nCR = near CR

* No statistically significant differences were identified between treatment arms.

Niesvizky R et al. *Proc ASH* 2010;**Abstract 619**.

Track 6

DR LOVE: How do you approach induction and long-term therapy for patients in the transplant setting?

DR NIESVIZKY: In both the transplant and nontransplant settings, achieving a complete remission is one of the most important goals that will be reflected in long-term survival and long-term progression-free survival. I believe the bar for complete response should be 40 percent, and I would reject any regimen that does not reach it.

Lenalidomide, dexamethasone and clarithromycin, or the BiRD regimen, yields more than a 90 percent overall response rate with an approximately 40 percent complete response rate (Niesvizky 2008). Similar results have been observed with lenalidomide/bortezomib/dexamethasone (Richardson 2010b). If we do not achieve a complete response or very good partial response with lenalidomide/dexamethasone, I add bortezomib to the regimen, either in combination with lenalidomide or in combination with cyclophosphamide and dexamethasone in a CyBorD approach.

With the new data coming from the CALGB and the French group, many physicians are considering continuation of maintenance lenalidomide after stem cell transplant (4.2).

4.2

Post-Transplant Lenalidomide Maintenance Therapy for Patients with Multiple Myeloma

	IFM 2005-02[1]		CALGB-100104[2]	
	Lenalidomide (n = 307)	**Placebo** (n = 307)	**Lenalidomide** (n = 231)	**Placebo** (n = 229)
Median PFS[1] or TTP[2]	42 mo	24 mo	42 mo	22 mo
Deaths	NR	NR	8%	12%

PFS = progression-free survival; TTP = time to progression; NR = not reported

[1] Attal M et al. *Proc ASH* 2010;**Abstract 310**; [2] McCarthy PL et al. *Proc ASH* 2010;**Abstract 37**.

Tracks 6-8

DR LOVE: Do you have any experience with the novel proteasome inhibitor carfilzomib or the new IMiD pomalidomide?

DR NIESVIZKY: At ASH, we heard the promising results of the Phase I/II study of front-line carfilzomib/lenalidomide and dexamethasone, with a 100 percent response rate when used for at least four cycles (Jakubowiak 2010). What is also significant is the reduction in neuropathy and the potential for long-term use. Pomalidomide has an excellent toxicity profile with less neuropathy, minimal thrombogenicity and improved responses when paired with dexamethasone (Lacy 2010). It also has the ability to overcome resistance to lenalidomide (Richardson 2010a). We're excited about this agent not only because of its efficacy but also because of its high level of tolerability. ■

SELECT PUBLICATIONS

Jakubowiak AJ et al. **Carfilzomib, lenalidomide, and dexamethasone in newly diagnosed multiple myeloma: Initial results of Phase I/II MMRC trial.** *Proc ASH* 2010;**Abstract 862**.

Lacy M et al. **Pomalidomide plus low-dose dexamethasone in myeloma refractory to both bortezomib and lenalidomide: Comparison of two dosing strategies in dual-refractory disease.** *Proc ASH* 2010;**Abstract 863**.

Niesvizky R et al. **BiRD (Biaxin [clarithromycin]/Revlimid [lenalidomide]/dexamethasone) combination therapy results in high complete- and overall-response rates in treatment-naïve symptomatic multiple myeloma.** *Blood* 2008;111(3):1101-9.

Richardson PG et al. **A Phase 1/2 multi-center, randomized, open label dose escalation study to determine the maximum tolerated dose, safety, and efficacy of pomalidomide alone or in combination with low-dose dexamethasone in patients with relapsed and refractory multiple myeloma who have received prior treatment that includes lenalidomide and bortezomib.** *Proc ASH* 2010a;**Abstract 864**.

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