INTERVIEW

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Tracks 1-15

Select Excerpts from the Interview

Track 4

DR LOVE: What are your thoughts regarding the new data presented at ASCO on maintenance lenalidomide for patients with MM after transplant?

DR PALUMBO: Unprecedented data were presented by two cooperative groups at ASCO 2010 (Attal 2010; [2.1]; McCarthy 2010; [2.2]) with lenalidomide maintenance therapy after autologous transplant in patients with MM.

Both studies showed that maintenance lenalidomide clearly provides clinical benefit by reducing the risk of progression by more than 50 percent. Additionally, the benefit occurs among all patients, not only those who achieve a partial response with transplant.

Maintenance therapy should be administered to all patients, independent of the response status after transplant.

2.1

Efficacy of Lenalidomide Maintenance After Transplant in Patients with Myeloma

	Placebo maintenance (n = 307)	Lenalidomide maintenance (n = 307)	Hazard ratio	*p*-value
Disease progression or death	143 (47%)	77 (25%)	—	—
Median progression-free survival (PFS)	24 months	Not reached	Not reported	$<10^{-7}$
Three-year postrandomization PFS	34%	68%	0.46	$<10^{-7}$

Attal M et al. *Proc ASCO* 2010;**Abstract 8018**.

2.2

CALGB-100104: Lenalidomide Maintenance versus Placebo After Transplant for Patients with Myeloma

	Placebo maintenance (n = 208)	Lenalidomide maintenance (n = 210)	Hazard ratio	*p*-value
Progression or death	58 (27.9%)	29 (13.8%)	0.42	<0.0001
Median time to progression	25.5 months	Not reached	Not reported	<0.0001

McCarthy P et al. *Proc ASCO* 2010;**Abstract 8017**.

Tracks 9-10

DR LOVE: What about lenalidomide maintenance for those patients with MM who are not eligible for transplant?

DR PALUMBO: Data on melphalan/prednisone with lenalidomide (MPR) followed by maintenance lenalidomide (MPR-R) have been presented (Palumbo 2009a; [2.3]), and this approach is clearly superior to melphalan/prednisone (MP) alone with a more than 50 percent reduced risk of disease progression.

In my view, maintenance therapy with lenalidomide is essential because it is providing more than 70 percent of this reduced risk of progression.

2.3

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

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 (HR = 0.499)

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

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

DR LOVE: Would you review your work on bortezomib-associated neuropathy, especially as it relates to the schedule of administration (Palumbo 2009b; [2.4])?

DR PALUMBO: Clearly no lack of efficacy was observed with a weekly bortezomib schedule versus a twice-weekly schedule in bortezomib/melphalan/prednisone (VMP) with or without thalidomide in terms of progression-free survival. Among elderly patients, the weekly schedule is now becoming the standard because higher-grade peripheral neuropathy is significantly reduced — from 14 to 18 percent with the twice-weekly schedule to two to four percent with the weekly schedule.

In addition to weekly scheduling, other issues to recognize are patients' education regarding the potential occurrence of neuropathy and bortezomib dose

2.4

Efficacy and Toxicity According to Bortezomib Infusion Schedule in a Phase III Study of VMPT versus VMP for Newly Diagnosed MM

	VMPT		VMP	
	Twice weekly (n = 71)	Weekly (n = 150)	Twice weekly (n = 64)	Weekly (n = 165)
Complete response	38%	32%	27%	20%
Grade III/IV peripheral neuropathy (PN)	18%	2%	14%	2%
Dose reduction due to PN	42%	11%	35%	13%
Discontinuation due to PN	10%	3%	15%	4%

Twenty-five patients receiving VMPT and 19 patients receiving VMP received both twice- and once-weekly bortezomib. V = bortezomib; M = melphalan; P = prednisone; T = thalidomide

Palumbo AP et al. *Proc ASCO* 2009b;**Abstract 8515**.

reduction, as needed. Bortezomib dose reduction to 50 percent should be considered when restarting after interruption for severe peripheral neuropathy.

Tracks 12, 14

DR LOVE: Would you discuss your trial of the four-drug regimen bortezomib, melphalan, prednisone and thalidomide (VMPT) followed by maintenance bortezomib/thalidomide (VT) for elderly patients with myeloma?

DR PALUMBO: This is an important study and showed that the four-drug combination VMPT followed by VT maintenance therapy is superior to VMP for progression-free survival (Palumbo 2010; [2.5]). The current standard three-drug regimens, such as MPR, melphalan, prednisone and bortezomib (MPV) and melphalan, prednisone and thalidomide (MPT), result in progression-free survival of approximately two years. With this background, the progression-free survival with VMPT followed by VT is clearly unprecedented and is increasing the remission duration by around one year. ■

2.5

Phase III Trial Comparing VMPT → VT to VMP Followed by Observation for Elderly Patients with MM

	VMPT → VT	VMP	*p*-value
CR	38%	24%	0.0008
≥VGPR	59%	50%	0.03
≥PR	89%	81%	0.01
Three-year PFS	54%	40%	0.006

CR = complete response; VGPR = very good partial response; PR = partial response; PFS = progression-free survival

Palumbo AP et al. Presentation. ASCO 2010;**Abstract 8013**.

SELECT PUBLICATIONS

Attal M et al. **Lenalidomide maintenance after transplantation for myeloma.** *Proc ASCO* 2010;**Abstract 8018**.

Blade J et al. **Criteria for evaluating disease response and progression in patients with multiple myeloma treated by high-dose therapy and haemopoietic stem cell transplantation. Myeloma Subcommittee of the EBMT. European Group for Blood and Marrow Transplant.** *Br J Haematol* 1998;102(5):1115-23.

McCarthy P et al. **Phase III Intergroup study of lenalidomide versus placebo maintenance therapy following single autologous stem cell transplant (ASCT) for multiple myeloma (MM): CALGB 100104.** *Proc ASCO* 2010;**Abstract 8017**.

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.** Presentation. ASH 2009a;**Abstract 613**.

Palumbo AP et al. **A phase III study of VMPT versus VMP in newly diagnosed elderly myeloma patients.** *Proc ASCO* 2009b;**Abstract 8515**.