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Does the amount of time one has to achieve treatment goals in the patient govern choice?

I am frequently asked, “Does the amount of time one has to achieve treatment goals in the patient govern choice?” I think this is an important clinical question that dictates the choice of therapies. Importantly, when we talk about the amount of time one has to achieve a treatment goal, it is dictated by the extent of underlying end-organ damage. For example, a patient with significant end-organ damage such as plasma cell leukemia, circulating plasma cells, significant hypercalcemia, or new onset acute renal failure, requires more aggressive therapy, in order to reverse the end-organ damage. We want to rapidly control the disease in these patients within the first 1 to 2 weeks of therapy. Controlling the tumor provides the best chance for patients to recover from their end-organ damage and, potentially, to return their renal function to baseline, as well as resolve their hypercalcemia. Those patients who need rapid disease control will dictate your choice of therapy, and will likely require a three-drug regimen. This will include carfilzomib, a proteasome inhibitor, plus an IMiD.

Importantly, a significant volume of new data presented at ASH 2015 demonstrated the superiority of three-drug regimens such as carfilzomib, lenalidomide and dexamethasone, or bortezomib, lenalidomide and dexamethasone over two-drug regimens such as lenalidomide and dexamethasone. There has been significant use of three-drug regimens over the last several years in myeloma, both with bortezomib-based regimens such as bortezomib/ lenalidomide/dexamethasone, as well as with carfilzomib-based regimens such as carfilzomib/lenalidomide/dexamethasone and carfilzomib/pomalidomide/dexamethasone, both in the newly diagnosed and in the relapsed/refractory setting. However, over the last year, we have importantly had clear confirmatory data with the SWOG 0777 study which demonstrated that lenalidomide/bortezomib/dexamethasone (LBD or RVD) is superior to lenalidomide and dexamethasone (LD or RD), both in response rates and progression-free and overall survival. Similarly, the ASPIRE study looked at carfilzomib/lenalidomide/ dexamethasone versus lenalidomide and dexamethasone. Both the SWOG 0777 and ASPIRE studies demonstrated that the combination of IMiDs and proteasome inhibitors are superior to IMiDs alone, as assessed by response rates, progression-free survival, and quality of life in both the newly diagnosed and relapsed setting.

As we move forward over the next year, it is clear that these three-drug combination regimens are becoming an important standard of care, both in our young transplant-eligible patients, as well as our transplant-ineligible older patients, as was seen in the SWOG S0777 study. In general, the amount of time you have to achieve treatment goals will dictate the choice of therapy, such that you may need to have more aggressive therapy for those patients with early end-organ damage in both the newly diagnosed and relapsed setting. We now have a significant amount of global data, however, suggesting that three-drug regimens may be the best option for all patients.

I hope this is helpful. Thank you for your attention. For additional resources, please view the other educational activities on *ManagingMyeloma.com*.