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What are truly myeloma defining events, and how will their assessment impact on clinical practice?

Welcome to *Managing Myeloma*. My name is Dr. Paul Richardson and I am the clinical program leader and director of clinical research at the Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute in Boston, Massachusetts. I am frequently asked, “What are truly myeloma defining events, and how will their assessment impact on clinical practice?” Now I think this is an extremely good question and a very important one as our treatment paradigm for this disease evolves. More and more now we are blessed with better, more effective, and better tolerated treatments. And in that context we are encouraged to use and think in terms of intervening with effective therapies sooner. The critical question is when can you so do this, when is too early, and arguably when is too late? In this context it is worth really noting that the so-called CRAB criteria are now largely considered somewhat obsolete. You should not be waiting for hypercalcemia, renal failure, severe anemia, and defining bone events before we initiate treatment. Having said that, there is the real entity of smoldering myeloma in which no treatment is indicated other than careful observation, and perhaps in the face of some minimal osteopenia, the use of a periodic infusion of bisphosphonate or something similar. Obviously this is a population also under active research study and these are patients in whom clinical trials should be encouraged. That being said, there are clearly a subgroup of patients who are now newly defined as having active disease who warrant therapy. And we have both single arm and phase 3 trials to support such interventions, not least of which was the original Spanish paper published in *The New England Journal of Medicine* a couple of years ago now, in smoldering myeloma which showed for the control arm, in what arguably has been defined as a more active population, a terrible outcome compared to the experimental arm of combining lenalidomide and dexamethasone. In this study, a survival benefit was shown supporting the further analysis of trials in smoldering myeloma. But on careful scrutiny, if we look at that control arm, we realize that they had features that might seriously suggest that they in fact truly have active disease. And if you look at this in the context of newer criteria that have been published by the International Myeloma Working Group, they are extremely helpful in understanding why earlier intervention is not only supportable by current data, but might actually be very important in improving patient outcome.

Now there is an excellent acronym for these new diagnostic features, and I think it is actually very helpful, and they are called SLIM. And what that means is that the patient must have 60% or more plasmacytosis, or an abnormal free-light ratio of ≥100, or have more than one lesion defined as being ≥5 mm on MRI or similar imaging. This is very important because this defines a population who previously might have been otherwise considered in the smoldering category in whom we would now consider to have reasonably active disease that is symptomatic and justifies therapy. Thank you for viewing this activity. For additional resources, please view the other educational activities on *ManagingMyeloma.com*.