How would you define and treat a myeloma patient with aggressive symptomatic relapse?

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Welcome to *Managing Myeloma*. My name is Dr. Robert Orlowski, and I am the Director of the Myeloma Section and the acting Chair of the Department of Lymphoma and Myeloma at the University of Texas MD Anderson Cancer Center in Houston, Texas. One of the questions that I get asked fairly frequently is, “How would I define an aggressive symptomatic relapse and what drug regimens would be recommended for treating a patient who is rapidly progressing?”

This is an important question because we do typically see two different patterns of relapse. One is a slow biochemical progression without clinical symptoms, and that can be treated less aggressively. Please look on the *Managing Myeloma* website for a different discussion of that scenario, I would define more aggressive relapse as somebody who has hypercalcemia; worsening renal function; worsening anemia; new bone lesions or previous bone lesions that are enlarging; extramedullary disease; a new plasmacytoma or an enlarging previously present plasmacytoma; or a rapid increase in the monoclonal protein or the free light chains in the serum or Bence-Jones protein levels. These are people with aggressive disease and you do want to be equally aggressive back, or the patients will become rapidly more symptomatic. What you do depends on what prior therapy the patients had and whether they are currently on maintenance or not. In general, in this kind of scenario, I like to introduce as many new drugs as possible. These would be drugs to which the patient's myeloma has either not been exposed at all, or maybe they have been exposed for only a brief period, such as during induction, and then the drugs were not reused during maintenance. There are several combinations that I think are very attractive in this setting. If, for example, a patient is progressing on lenalidomide maintenance, then options would be to use carfilzomib with pomalidomide and dexamethasone, or something like daratumumab with bortezomib and dexamethasone. If you have a patient on a proteasome inhibitor maintenance (this could be bortezomib or ixazomib, for example) then either pomalidomide or lenalidomide with daratumumab and dexamethasone would be very reasonable. I also like pomalidomide with elotuzumab, or lenalidomide with elotuzumab, both with corticosteroids, for patients who are progressing on proteasome inhibitor-based therapies. Other combinations that you can consider would include panobinostat, which is effective and approved with bortezomib, but also very effective and may be even better-tolerated in combination with carfilzomib. I often will use other drugs like bendamustine or cyclophosphamide or pegylated liposomal doxorubicin, usually in combination with proteasome inhibitors, and these are some of the options that you can use for more aggressive disease. The goal is to try to get control of the aggressive disease and either then take patients on to either a first or second autologous transplant, or if that is not an option, try to get them down to the lowest level of disease possible – hopefully MRD or minimal residual disease negativity – and then maybe peel back some of the drugs and drug dosing to leave patients on a more tolerable long-term, maintenance-type regimen. I hope that this has been helpful in managing your more aggressive patients with relapsing myeloma, and thank you for viewing this activity.