What factors do you consider when choosing treatment in newly diagnosed multiple myeloma?

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Welcome to *Managing Myeloma*, I am Dr. Shaji Kumar. Today I would like to discuss the factors to consider when deciding on treatment choice in newly diagnosed multiple myeloma.

The treatment choices for multiple myeloma have significantly expanded with the introduction of multiple new drug classes. Several factors related to the patient, as well as the disease, should be taken into consideration when deciding on the initial treatment for multiple myeloma. One of the most important factors is the age of the patient and the eligibility to undergo an autologous stem cell transplant. In patients who are eligible to go through a stem cell transplant, the typical regimen that we would start with is one that includes bortezomib, lenalidomide, and dexamethasone (VRd). This is based on phase 3 trials demonstrating an improved overall survival for patients on this regimen. In patients who are transplant eligible and have high-risk disease, we could certainly consider using some of the newer drugs, proteasome inhibitors like carfilzomib, with lenalidomide, and dexamethasone (KRd); but this should be based on risk stratification based on FISH-based testing demonstrating high-risk abnormalities like 17p deletion, t(4;14) or t(14;16). In patients who are ineligible to undergo an autologous stem cell transplant, we could consider using the same three-drug combination (VRd) but using lower doses of the drugs or using a schedule that is more stretched out (so the intensity of the therapy is lower). If the patients are too frail to use a three-drug combination, we can certainly consider using a lenalidomide-dexamethasone regimen for those patients if they are standard risk, or a bortezomib-based regimen if the patients have high-risk disease.

There are other host-related factors that have to be taken into account when deciding on therapy. In addition to age, this also includes renal function. If a patient presents with a renal insufficiency, the choice of the drugs may have to be altered based on the drug metabolism. We would use a combination of bortezomib with cyclophosphamide-dexamethasone or thalidomide-dexamethasone in patients who present with significant renal dysfunction. Patients who are requiring hemodialysis certainly should be immediately initiated on hemodialysis while they are being started on the systemic therapy for their multiple myeloma. There is some controversy as far as the use of plasma exchange in these patients, but it is certainly something reasonable to consider, especially in those patients who present with high levels of serum-free light chain. Patients who present with significant extramedullary disease or plasma cell leukemia may have to be treated with more aggressive chemotherapy-based combinations such as the bortezomib, doxorubicin, dexamethasone (VDd)-based regimen, or other multidrug combinations that can allow us to bring the disease under rapid control.

The goals with the initial therapy are many-fold. We do want to get the disease under control as soon as possible so that the disease-related complications can be reversed, particularly

complications such as renal failure. We also want to decrease the risk of infections because these patients are at a high risk of infections and early mortality. By controlling the disease rapidly and reversing the disease-related complications, we significantly decrease the risk of infections and risk of death related to the complications. It is also important that we take into account the fact that we need to collect stem cells in the transplant-eligible patients. We know that combinations such as bortezomib-lenalidomide-dexamethasone – especially when used for four to six cycles – do not interfere significantly with the ability to collect stem cells. If patients – especially older patients – are continued on lenalidomide beyond six cycles of therapy, it could impact the ability to collect stem cells, and this also needs to be considered when you decide on the timing of stem cell collection.