Managing Myeloma

Abstract 141

Selinexor, Pomalidomide, and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma

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Welcome to *Managing Myeloma*. I'm Dr. Saad Usmani, and I'm live at the 61st ASH conference in Orlando, Florida. Today, I will be reviewing the results of the oral presentation titled "Selinexor, Pomalidomide, and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma." Selinexor is an oral XPO1 inhibitor. It's a novel mechanism of action that was FDA approved in July of 2019 in combination with dexamethasone for triple-class refractory multiple myeloma, and now there are several combinations that are being examined and that includes the combination of pomalidomide and dexamethasone. So, let's take a deeper dive into this particular phase 1 study that finished accrual earlier this year for the dose escalation cohorts. Forty-eight patients were enrolled in the study with a median age of 64 and a median prior lines of four treatment regimens, 83% of the patients had received a prior autologous stem cell transplant and one patient had also received an autologous and allogenic stem cell transplant. Overall, across the different cohorts of patients, eight DLTs were observed and they were primarily related to fatigue, febrile neutropenia, and thrombocytopenia. And we already know that these AEs do occur with both selinexor and pomalidomide and would be expected. So, we didn't see any unexpected DLTs across these cohorts.

Overall, the common hematologic treatment-related adverse events included neutropenia at 54% for grade 3 or higher, thrombocytopenia at 33%, anemia at 29%, and leukopenia at 15%, and common non-hematologic treatment-related adverse events included nausea, fatigue, diarrhea, and vomiting, but majority of these appear to be grade 1 and 2, and there were lower rates of grade 3 or higher thrombocytopenia that were observed in the Q-weekly dose versus the biweekly dose. So, this particular part was informative and will likely impact how this combination moves forward in randomized phase 3 studies.

So overall, in terms of response, 44 of the 48 patients were evaluable for the response, 27 patients had prior refractoriness to lenalidomide and were pom-naive, four patients were lenalidomide treated or exposed and pom-naive, 13 patients were refractory to both pomalidomide and lenalidomide, 19 patients were refractory to lenalidomide as well as bortezomib. So in this patient population that was pomalidomide-naive, the overall response rate was 58% with 7 VGPRs and 11 PRs and a median PFS of 12.2 months. For the patients who were refractory to lenalidomide and pomalidomide, the overall response rate was still impressive at 31% and included 4 PRs and the median PFS was 4.2 months.

So, this study is very informative. XPO1 inhibition is a novel mechanism, pomalidomide is a very effective immunomodulatory drug; and both of these drugs have good CNS penetration as well.

We're looking forward to seeing this regimen make it to randomized phase 3 studies so that we can eventually use this for our patients. At this point in time, from a community practitioner perspective, I wouldn't recommend utilizing this regimen, but be on the lookout for the phase 3 data that should be forthcoming in the next couple of years.

Thank you for your attention.