Managing Myeloma

How do I dose daratumumab, bortezomib and dexamethasone in the combination regimen?

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Hi, I am Dr. Carol Ann Huff. Over the next few minutes, I will discuss with you how I dose bortezomib and dexamethasone in conjunction with daratumumab in patients with multiple myeloma. This regimen has been found to be superior to the administration of bortezomib and dexamethasone alone, which was published in the CASTOR trial in the Fall of 2016 in the *New England Journal of Medicine* by Palumbo and colleagues.

In the **labeled indication** for bortezomib and dexamethasone in conjunction with daratumumab, bortezomib is dosed on the traditional day 1, 4, 8, and 11, every 21-day schedule at a dose of 1.3 mg/m^2. I, however, administer the bortezomib at a slightly higher dose of 1.6 mg/m^2 subcutaneously, days 1 and 8, every 21 days. The reason for this difference is that data in other trials has shown that there has been similar efficacy, with a lower incidence of peripheral neuropathy. Many of these patients already have peripheral neuropathy from prior administration of anti-myeloma therapies, which might also include bortezomib, and I have found that this has been equally efficacious with less risk of toxicity.

Daratumumab in Combination with Bortezomib, Dexamethasone

- First three doses are given on an every 3-week schedule
- Daratumumab is given at the standard dose of 16 mg/kg once a week for 9 weeks continuously (or three full 3-week cycles)
- Followed by cycles 4 through 8 being every 3 weeks, with the daratumumab given on day 1 of each of those cycles
- The bortezomib is given weekly for days 1 and 8 out of every 21 days for the 8 cycles of therapy
- Cycles 9 and beyond, daratumumab is given once every 4 weeks at the dose of 16 mg/kg, as published in the CASTOR trial
- Bortezomib is discontinued after cycle 8
- Dexamethasone is given at a dose of 20 mg to 40 mg orally on days 1 and 8 of the 3-week cycle for the first 8 cycles of treatment

In addition to the premedications that are indicated in the package insert for daratumumab, which are methylprednisolone, acetaminophen, and an antihistamine, we

have found that it has been helpful to add in montelukast; 10 mg orally on the days of infusion of daratumumab, for the first 2 to 3 cycles, to help reduce the incidence of infusion-related reactions, allowing the ease of administration of the daratumumab. This three-agent combination has been found to be highly effective in patients with relapsed multiple myeloma and can be readily administered in an outpatient setting to the majority of patients.