Subcutaneous Velcade Leads To Similar Response Rates, But Fewer Side Effects, Compared To IV Velcade In Newly Diagnosed Multiple Myeloma

By The Myeloma Beacon Staff
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Initial results of a German clinical trial confirm previous findings that subcutaneous (under-the-skin) injections of Velcade for the treatment of myeloma lead to fewer side effects – but similar overall response rates – compared to intravenous (IV) infusions of the drug.

The trial results also indicate, however, that IV administration of Velcade may lead to deeper treatment responses when patients are given the drug for a limited number of treatment cycles.

The German trial is notable not just because it is the largest study to date that has directly compared subcutaneous and IV Velcade. It also is the first study of its kind to be carried out in newly diagnosed myeloma patients. A previous study that compared the two methods of administering Velcade was conducted with relapsed myeloma patients.

In addition, the German study compared subcutaneous and IV Velcade when used as part of two different multi-drug treatment regimens. One of those regimens is the commonly used combination of Velcade, cyclophosphamide, and dexamethasone (VCD, CyBorD).

In the previous comparative study involving relapsed patients, treatment initially was with Velcade alone. Dexamethasone could be added to the Velcade if, after four initial cycles of treatment, patients did not achieve a complete response.

The results of the German trial also indicate that responses to treatment with subcutaneous and IV Velcade were similar in three patient subgroups the researchers analyzed regularly throughout their study: patients with chromosomal abnormalities associated with higher-risk disease; patients with reduced kidney function; and patients with Stage III disease at diagnosis.

The new trial results are not, however, an unequivocal victory for subcutaneous Velcade. Although response rates for subcutaneous and IV Velcade were similar in the trial, the share of patients achieving deeper responses was higher in patients treated with IV Velcade.

For example, among the patients in the trial who received the VCD treatment regimen, 42 percent of those who received IV Velcade achieved at least a very good partial response, compared to 29 percent of the patients who received subcutaneous Velcade.

This difference in depth of response was not seen in the earlier comparative trial with relapsed patients. In that study, depth of response was almost exactly the same in both the subcutaneous and IV patients.

It is possible that the difference in depth of response in the German trial was due to the fact that patients in the trial received only three cycles of each of the tested treatment regimens. Had the patients received additional cycles of treatment, the German researchers note, there may not have been much difference in depth of response.

In the earlier comparative trial, the relapsed patients participating in the study could receive up to 10 cycles of therapy. Other studies also have examined the efficacy and tolerability of subcutaneous Velcade, although they have not included comparison groups of patients treated with IV Velcade. These other studies, the German researchers add, also involved more than three cycles of therapy, and their results suggest that subcutaneous Velcade does not result in less depth of response than IV Velcade.

Significance Of The New Study

"The German study's results regarding potential differences in depth of response between subcutaneously and intravenously administered bortezomib [Velcade] as part of multi-drug combinations are really quite interesting," Dr. Paul Richardson of the Dana-Farber Cancer Institute in Boston told The Beacon. "The results may in fact have some significance in clinical practice."

"IV administration is known to lead to higher peak concentrations of bortezomib in a patient's blood, as compared to subcutaneous administration," Dr. Richardson went on to explain. "The higher concentration has resulted in more effective treatment of plasmacytomas in preclinical models, and this may explain the greater efficacy of IV, rather than subcutaneous, bortezomib sometimes seen in patients with advanced myeloma and extramedullary plasmacytomas."

"IV bortezomib therefore could be of importance," Dr. Richardson elaborated, "in select patients who do not initially benefit from subcutaneous administration – especially those with refractory, bulky disease requiring a combination approach."

That said, Dr. Richardson also agreed with the authors of the German study, who noted that, because subcutaneous administration of Velcade results in significantly fewer serious side effects than IV administration, it should allow the drug to be given for a greater number of treatment cycles in many patients. This, in turn, could allow for deeper responses over time than were seen in the new study, with its fixed number of three initial treatment cycles.