Managing Myeloma

The Connect® MM Registry Trial: Results Across the Disease Spectrum

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Welcome to *Managing Myeloma*. My name is Dr. Philip McCarthy, and I am Professor of Oncology and Internal Medicine and Director of the Blood and Marrow Transplant Program at Roswell Park Cancer Institute in Buffalo, New York. I am here to talk about some registry trials. One is sponsored by Celgene Therapeutics, and what they demonstrate is that they are able to collect a large amount of data from patients in the community who are receiving therapy for multiple myeloma, and this is called the Connect MM Registry. They looked at treatment outcomes and health care resource utilization in patients with newly diagnosed multiple myeloma who had received a variety of different induction therapies. These patients then may or may not have received transplant, and may or may not have received lenalidomide maintenance. What they were able to show is that, number one, there are still a significant number of patients who are considered transplant-eligible but who actually do not go on to transplant therapy as part of their first treatment after induction. This is important in terms of what we found based on the recent determination trial that was published in the *New England Journal of Medicine* (Atallah, et al.) a couple of months ago. What they showed was there was a 14 month progression-free survival benefit for the patients who received stem-cell transplant upfront versus those who had deferred and continued chemotherapy. Now, there is no difference in overall survival, and that is good, and what it could mean is that there won't be in the future. However, we do not know what happens because the majority of patients still have not relapsed, and the overall survival at three years is over 80%, which is fantastic. We are going to have to wait several years to see on that trial what are the outcomes from transplant versus chemotherapy and then lenalidomide maintenance. However, we have this Connect MM Registry which gives us an idea of what it is like in the community, and what we see is that there is definitely a benefit to lenalidomide maintenance versus no maintenance.

Now, another interesting thing is they did a quality of life study on health care resource utilization. They found that patients receiving lenalidomide maintenance did not have a major impact on their quality of life. Now, this is not a randomized trial, so it is useful from a registry standpoint, but what we will need to do for future trials is to have quality of life instruments built in to maintenance therapy trials that will allows us to determine the effect of prolonged maintenance therapy on the patient's quality of life.

Another interesting aspect of the Connect Multiple Myeloma Registry is the impact of a chromosome 11;14 abnormality on survival outcomes in African American patients. What they showed is that patients who are African American and who had an 11;14

translocation at diagnosis had an inferior progression-free and overall survival when compared to non-African American patients with the same chromosome abnormality. Now, this is quite interesting. It is not entirely based on a certain fact. In other words is this a racial characteristic feature, genetic characteristic, or some other impact that we do not understand? The thing that is exciting about this though is that there is now venetoclax,* which is an oral BCL-2 inhibitor, and has a particular benefit in patients who have the 11;14 abnormality. Right now, venetoclax is used for the treatment of CLL, and there are clinical trials examining its benefit in a phase 3 manner. In terms of off-label use, this may be the patient population in the relapsed setting for whom venetoclax should be considered. This remains to be determined based on insurance coverage, drug availability, and a variety of other factors, but this may allow us to better determine outcome in this patient population.

One thing that is really important is that we should be thinking about repeating bone marrow tests on patients, especially when they have disease progression, and this is because we find that new cytogenic abnormalities may arise over time in the patient. Myeloma is very different from a lot of the other hematologic disorders in that there are clonal abnormalities that will pop up. It is kind of like whack-a-mole when one clone gets knocked done and another clone arises. Now that we have drugs that may overcome particular cytogenic abnormalities, it really behooves us to think about repeating bone marrow tests. Not every month, but in particular progressions, and not relying solely on laboratory tests to determine whether or not a patient may or may not be progressing. The field of myeloma continues to evolve. Now that we have all these new agents, it is hard to figure out how to sequence them in the relapsed/refractory setting. We are beginning to move them up into the upfront setting - so that is another question - but in the relapsed/refractory setting, we now have three uses for daratumumab. You can use it with bortezomib and dexamethasone, you can use with lenalidomide and dexamethasone, or you can now (just FDA-approved) use it with pomalidomide and dexamethasone. We are going to have to figure out how all these things work together. One good thing about these registry studies is it allows investigators to get a feel for what it is like in the community, how patients are being treated, and how can we better optimize treatment for our patients with the goal someday of curing them of their disease. Thank you very much for viewing this activity. This is Philip McCarthy speaking to you today from the European Hematology Association in Madrid, Spain, 2017.

* Venetoclax is not approved by the FDA for use in patients with multiple myeloma.