Expert Shares Key Takeaways From 2019 International Myeloma Workshop

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Cindy Chmielewski:
Hello, everyone. My name is Cindy Chmielewski. I'm a patient engagement specialist here at Patient Power, and I'm a myeloma patient and patient advocate. Today I have the pleasure of speaking with Dr. Larry Anderson. We're going to be talking about the International Myeloma Workshop, which happened just recently in Boston where over 3,000 myeloma specialists gathered learning about the biggest and greatest happenings in myeloma.

What do you think were some of the key findings from this meeting?

Dr. Anderson:
First of all, just the biggest key point, as you noted, over 3,200 attendees from 41 countries, so there's a big interest in what's going on in myeloma, and these are just the specialists and pharmaceutical company people and patients and other people that are just specifically interested in myeloma from all over the world. So each—or every other year as we have this conference it continues to grow and grow, so hopefully that will continue.

As far as the data that was presented I think some of the key data updates were from the Griffin Study that I mentioned, which is looking at moving daratumumab (Darzalex) up front along with RVD or lenalidomide bortezomib dexamathasone (Revlimid Velcade Devcadrom) and induction therapy for transplant patients. You may recall we recently had a FDA approval of Darzalex Revlimid and dexamethasone for the nontransplant patients within the past few months, so those patients already can get Darzalex up front, but as far as combining Darzalex with RVD, the GRIFFIN Study is looking at that question, so essentially triplet therapy versus quadruplet with the fourth drug being a monoclonal antibody that targets CD38 called Darzalex.

And this study randomized patients between Revlimid and Velcade and dex triple therapy with or without adding Darzalex. And this adding Darzalex to this combination significantly improved the depth of these responses, significantly more stringent complete responses with this combination, and also of note much higher rate of molecular remissions or MRD negative, minimal residual disease negativity, which can't be seen in many regimens, but now that we're combining monoclonal antibody with our other novel therapies in myeloma we're starting to see very deep remissions.

We're still awaiting further follow-up to know if that translates into longer remissions and longer survival, but so far so good. So that was the Griffin data.

Also there was an update of the Cassiopeia, which is a very similar study mostly done in Europe, adding Darzalex to the Velcade thalidomide and dexamethasone background, so dara BTD versus BTD. So instead of using Revlimid they're using thalidomide in the studies in Europe. So we don't use a lot of thalidomide (Thalomid) in the US, but it is a very important

study. And actually just a few days ago based on this study the FDA has approved Darzalex BTD combination here in the United States as well.

But at the IMW meeting the update was looking specifically at the high-risk patients that have deletion 17p or translocation 414 or really high-stage myeloma, and found that the rates of remission and the molecular or MRD negativity was also deepened in the high-risk group. Some would fear that even with the Darzalex-based combinations we're not necessarily seeing great remissions in high-risk patients unless we add in proteasome inhibitors.

So a lot of patients that have high-risk disease we may not necessary want to use just the Darzalex and Revlimid, but now that we're combining proteasome inhibitors with that combination, whether it's dara BTD or dara RBD, it does look there's a signal for improvement in outcomes in those high-risk patients. Further time will be needed to follow-up on that and see if that pans out to better survival, but it's a good start.

One of the other key takeaways was an update of the Dream Study, so some of the most exciting trials that are ongoing in myeloma are targeting this protein on the surface of plasma cells called BCMA or B-cell maturation antigen, so there are many different ways of targeting that. Some studies are using gene modified or CAR T-cells. Some are using BiTE therapy, BiTE-specific T-cell engager, but in the Dream Study they're using the antibody drug conjugate antibody, so it's basically an antibody with a toxin conjugated to it to directly target the myeloma cells and target them for destruction.

So we've already known that that molecule has good response rates, but in this study essentially they're further following that up and confirming good response rates but also the key thing for me is there is some preliminary data now that we can actually split the first dose over two weeks and have less corneal toxicity. As you may recall, one of the main toxicities of that therapy with the every-three-week dosing was corneal toxicity, and now that there's some preliminary data on splitting the dose I'm hopeful that that will pan out and those patients will be able to receive that therapy without any significant corneal toxicity.

Also, further updates from, as I mentioned, the bi-specific T-cell engagements therapy is another potential way of targeting that same target, the BCMA. There was an update on the AMG 420 BiTE therapy in myeloma which confirms excellent response rates, also now some data on MRD negative or minimal residual disease negative testing in those patients, so very exciting.

Also some newer drugs that are showing promise that are things that we don't have available right now. One would be the melflufen alkylating agent has really good responses and acceptable, reasonable toxicity as well as the sort of a fourth-generation IMiD. Now they're calling it CELMoD, so the iberdomide or CC 220 data looks very promising.

Also looking at targets—data looking at targets that we haven't really seen much on, for example, the Mcl-1 inhibitor known as the AMG 176 looks very promising. So a lot of different targets or molecules coming down the pipeline that just makes it exciting times in myeloma.

Another exciting thing is not only therapeutic but the imaging that we do in myeloma currently relies on CAT scans and MRIs and then PET scans. Current PET scan technology used as sort of a radio labeled or tracer sugar molecule that gets taken up by active growing tumor in myeloma, whereas now at this conference some data was presented on using an anti-CD 38 antibody that has a radio tracer on it so that that can light up wherever there's active plasma cell tumor.

So that is exciting, which just means that you could probably use any sort of plasma-cell-targeted antibody and have much better visibility of where all the tumor cells are. Even if they're not actively growing they could potentially find them better with these antibody-directed PET scans.

Cindy Chmielewski:
Do you think any of the studies will be practice changing?

Dr. Anderson:
I think as it stands right now they're more hypothesis generating and early-data generating, not necessarily things that we'll use to change our practice tomorrow, but incrementally will be part of our practice changing data. I agree. Most of

the things that they were debating, therapy for smoldering myeloma, right now should be probably on a clinical trial. A lot of the other controversial things, you know, how do we use MRD testing? Can we use it to stop therapy if they're MRD negative? I don't think we have any data for that. If we're MRD-positive, should we use that to augment their therapy? Current studies are ongoing looking at those questions.

So I agree. I don't think necessarily we have practice-changing information at the moment, but incrementally this will be used as part of that.

Cindy Chmielewski:
With all this information that patients have, how could knowing what happened at a meeting such as the IMW help empower patients to have discussions with their doctors?

Dr. Anderson:
Yeah, so if they know that these meetings are going on and some of the takeaway points they can ask their doctor, hey, do you have a trial with this drug? Do you have information on when this might be available? So am I on the latest treatment options? Am I on the therapy that's still appropriate? And for newly diagnosed patients those therapies are changing every few months, and so just staying up to date on what the current data is.

Cindy Chmielewski:
Exactly. And I guess it's an important point to make that at any point of your treatment journey that you probably should be asking about clinical trials because some of those drugs may only be available to you through a clinical trial.

Dr. Anderson:
Correct. Yeah, it might be years before they're available from FDA approval, but you could potentially get that drug now through a trial. And also with clinical trials a lot of patients think, oh, I have to be relapsed and refractory or falling off the wheels to get on a trial, but no. We have many trials for newly diagnosed patients, for smoldering patients. You don't have to be falling apart to want to consider a clinical trial.