Myeloma News From ASH 2018: Updates on CAR-T Therapy, Antibody Drug Conjugates and Maintenance Strategies

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Esther Schorr:
Hello to everybody. This is Esther Schorr with Patient Power, and I'm here today at the 2018 ASH conference, the American Society of Hematology. And I'm surrounded by, oh, 20-, 25,000 amazing researchers and clinicians who are studying hematological malignancies. And I have about me today Dr. Amrita Krishnan. Is that correct?

Dr. Krishnan:
That's correct.

Esther Schorr:
And she is the Director of the Multiple Myeloma Program at the City of Hope in Los Angeles. Thank you for being here. So what I wanted to talk to you about today is what's going on for myeloma patients. What are the headlines from ASH this year?

Dr. Krishnan:
Good morning, Esther. Thank you for the opportunity to talk. I don't even know where to begin. There's—every myeloma session has been packed, standing room only, which tells you obviously, number one, the advances we're making and the enthusiasm regarding them.

I'd say the three biggest news really is obviously CAR-T cells in relapsed disease, and we started out just hearing about one CAR-T construct, the BB121. Now we obviously are hearing many other companies presenting their results and other CAR-T constructs, which I think is very good for us because we can understand better both the technology as well as side effects and efficacy and understanding among different T-cell constructs.

The other big thing, I would say, antibody drug conjugates by specific antibodies. And then the last but not least let's not forget in terms of stem cell transplantation there was a big session this morning looking at new drugs in the maintenance setting, so specifically oral proteasome inhibitors.

Esther Schorr:
Oh, boy. Okay. So now I'm going to drill down a little bit from a lay person's standpoint about what you just said.

Dr. Krishnan:
Okay.

Esther Schorr:
It's a lot of alphabet soup. So I know that you've been doing some work with the drug daratumumab (Darzalex). It's a mouthful, and I know that that's a monoclonal antibody. And can you talk a little bit about what the relevance is about that? Because I think our audience has probably heard of it but doesn't know what's happening in that area.

Dr. Krishnan:
Sure, happy to. So daratumumab targets CD38, which is a protein on the myeloma cell. So it's very specific in terms of attacking the myeloma cell. Now, that protein is expressed in other things like red blood cells, but really it's very highly expressed on plasma cells, sort of the myeloma cell per se. So daratumumab was already approved for relapsed myeloma, both multiply relapsed as well as patients who have a first relapse in myeloma in combination with some of the other drugs we think about such as bortezomib (Velcade) or lenalidomide (Revlimid).

This meeting this year, though, the big excitement is in regards to using daratumumab in newly diagnosed myeloma. So we already know it's a very effective drug in the relapsed setting. We're familiar with the toxicity profile, and overall it's quite well tolerated, and so now the question becomes if it's such a good drug should we move it earlier in the course of therapy to get the maximum benefit.

Esther Schorr:
So it could be a first-line therapy.

Dr. Krishnan:
Exactly. So it's already approved in the first-line setting in combination with Velcade, melphalan (Alkeran) and prednisone (Deltasone), so VMP, but that's not a regimen we use in the United States. So there's going to be an abstract presented Tuesday, so I can't even tell you yet because it's a late breaker, but we only know a little hint of it which is using daratumumab plus lenalidomide and dexamethasone in newly diagnosed patients. It's called the MAIA study, and that's the one that we're all waiting to hear to see is that going to establish a new standard of care in the newly diagnosed front-line setting.

Esther Schorr:
So that helps me to understand that, thank you. So then are there other studies that you're involved in that would be interesting for patients to know about?

Dr. Krishnan:
So there's another study that actually was presented yesterday. It's called the Griffin study. That uses daratumumab in combination with sort of I would say a quote/unquote standard regimen in the United States, RVD or lenalidomide, Velcade and dexamethasone (Decadron). And what it asks again the same question. If you add to our standard backbone another potent agent, does it even further improve the responses? So what they presented on Saturday was very early data on 16 patients, so we need to wait more, but it just shows you the excitement around that. And

that data they presented really was around the safety and suggesting that it's a well-tolerated combination with a very high response rate, 100 percent response rate.

Esther Schorr:
Well, that would be my question then just as a care partner myself is when you're talking about doing those kinds of combinations of two, three, four drugs are you all looking at the combined toxicity of those things and the side effects?

Dr. Krishnan:
Oh, yes, absolutely. So the MAIA study, for example, very specifically looked at the three drugs of daratumumab plus len-dex comparing it to the two drugs, lenalidomide and dexamethasone, so--and the same thing with the GRIFFIN study. That also was randomized so half the people got daratumumab in combination, the other half just got the standard RVD.

And there was, to be fair, a lightly higher increase in side effects when you added the daratumumab, a bit more infections and a bit more blood toxicity, so lower white counts. So it is something to sort of, you know, take as a note of caution too, when you add more drugs that you do certainly expect that you are going to get more toxicity. And obviously it becomes does the benefit outweigh the potential risk.

Esther Schorr:
As usual. So I guess the other question I have is where does stem cell transplantation fit in all of this, or does it?

Dr. Krishnan:
So obviously I have a somewhat biased opinion. I come from City of Hope, which is the largest transplant center in California, and two things I could say in terms of myeloma. So we do over 8,000 transplants a year in the United States for myeloma, so it suggests that it's a standards of care backbone of therapy.

As a transplanter I would say transplant still has the longest track record in terms of remission length and even if you compare it to standard RVD chemotherapy you get a longer remission when you throw transplant into that mix. And I think what will be of interest to us is further improving upon that by either different maintenance strategies or induction strategies, so new treatment before the transplant as well to further improve the outcomes of the transplant.

And then the other thing I should mention, this is not a study that is open yet but it's a study that we actually had some meetings about through the BMTCTCN, so a cooperative group of transplant networks, trying to ask the question. So this is a group—you know, I used to chair the myeloma committee, and I'm still on the committee—we try and look ahead. Right? So we say, what can we do as a strength of network of transplant centers that patients really need? What is the question they want to ask? And one of the unmet needs is high risk-myeloma. So whatever we do right now, and there's been data presented at this meeting too, we need to do better.

For those patients who have advanced stage of myeloma, high-risk cytogenetic abnormalities, the therapy we have right now is still not optimal. And one of the things that we're going to do that we're very excited about is we're going to open a study that we're literally going to go home and start writing in January, using CAR-T cells after an autologous transplant for patients with high-risk myeloma.

Esther Schorr:
So that gives—that's hope for patients that have not had any real viable treatments till now or durable ones.

Dr. Krishnan:
I think that durable is what we would say. So we're all very excited about that. It's going to harness our strengths as transplanters, our strengths in cellular therapy and CAR-T and moving it up front.

Esther Schorr:
Good. Well, thank you, Dr. Krishnan for all the work that you and your associates are doing. I know that it's, especially for myeloma patients and their families, it's so important. So thank you.

This is Esther Schorr from San Diego at the ASH conference. Remember, knowledge can be the best medicine of all.