Myeloma Treatment Classes

Recorded on: September 29, 2012

Sagar Lonial, M.D.
Associate Professor at Winship Cancer Institute of Emory University
Director, Translational Research, Emory Healthcare

Craig Hofmeister, M.D.
Assistant Professor
Ohio State University Comprehensive Cancer Center

Andrew Schorr:

We talked about the medicines, so how do the medicines fix that or knock that back? And maybe you can talk about the different classes. How do we understand how they work?

Dr. Lonial:

Okay. You guys are going to walk out with your junior M.D. degrees then by the end of the day. All right.

Dr. Hofmeister:

Who needs med school when you've got Google, right?

Dr. Lonial:

That's right. I think there are three big classes of drugs that we can—four, probably, if you want to think about it. I'll take two, and I'll let you take two, how about that?

Dr. Hofmeister:

Please.

Dr. Lonial:

I'll take probably one of the oldest classes that we've used, and that's corticosteroids, and this is the one that nobody likes to take. Prednisone or Decadron, many of you have probably heard

those, or dexamethasone. And those are steroids, not the steroids that the cyclists use when they try and win the Tour de France, but the steroids that are actually part of sometimes an immune response, or steroids are basically what we use to make lymphocytes, B-cells and T-cells go away. We know that steroids themselves can kill myeloma cells. When you're getting dexamethasone (Decadron) or prednisone it's not because we want to make your life miserable, it's because we know these drugs kill myeloma cells.

The second class I'll take is the proteasome inhibitors, and the proteasome inhibitors include Velcade, or bortezomib, and it includes carfilzomib, or Kyprolis, the new one. And this is really one of the first drugs that brought us to the new era of myeloma therapy, mostly because they target something in myeloma cells that is really unique to myeloma as a cancer. And remember I told you the main purpose of a plasma cell is to make antibody. And by making antibody, loads and loads of antibody, plasma cells have to figure out how to manage extra protein within their cells.

And the proteasome is a garbage disposal within each and every one of our cells, and by blocking the proteasome, by taking the garbage can out, the cell doesn't know what to do with the proteins that are not normal or bad. And when you don't know what to do with them they build up and build up, and when they build up it eventually kills the cell. Basically myeloma cells are set up to be dependent on the proteasome, and by taking it away with a drug like Velcade or carfilzomib you take away that ability to deal with excess protein. And that is critical for myeloma cell survival.

All right. You're up.

Andrew Schorr:

Okay. IMIDs.

Dr. Hofmeister:

So iMIDs are immune modulators, and I've always chafed at that because the immune modulation is hard for most people to appreciate because when they get immune modulating drugs like Revlimid (lenalidomide) or thalidomide (Thalomid) it's often immunosuppressive to them.

Now, thalidomide (Thalomid) started out kind of checkered history, right? Used for nausea in pregnancy decades ago and ended up being discovered to cause birth defects. And it took roughly 60 years for scientists to discover exactly what it was that led to that birth defect, but in the interim a patient and a patient advocate brought thalidomide (Thalomid) back to the US and said, Hey, my loved one is dying of myeloma. This could be an angiogenesis drug. This could decrease the blood vessel supply to the tumor. And they gave thalidomide (Thalomid) to that patient and they did well. And thalidomide (Thalomid) then led to an improvement of more effective drugs with less side effects called Revlimid (lenalidomide), which has led to another improvement, a more

effective drug with less side effects called pomalidomide (Actimid). And these drugs all bind to a particular protein in the myeloma cell and basically stop it producing so rapidly.

When there are four drug classes in myeloma, the proteasome inhibitors, the steroids, iMIDs are the third important class and if you have a peanut and jelly analogy here, peanut butter—proteasome inhibitors, iMIDs and steroids, they just go together so nice.

And the alkylators, or the standard chemotherapy, for this, this is the melphalans, this is the Cytoxans, this is the old-time chemo. This is the type of therapy where dose is most important. The higher the dose, the more effective the drug will be with any cancer cell it's exposed to. Unfortunately, it affects normal cells, too, and our most commonly used chemotherapy drug is called melphalan (Alkeran). We use it in the setting primarily in high doses just prior or coincident with an autologous transplant.

And transplant, for those of you are not familiar, and many of you unfortunately and fortunately are, doesn't involve any surgery, there's no operating room, we're not moving organs from one patient to another. A transplant is essentially a way to give patients high-dose IV melphalan (Alkeran) safely, then 48 hours later they get some of their own stem cells back through an IV to almost soothe the bone marrow from all these toxic melphalan (Alkeran) and recover their counts more quickly than they would normally.

Those four classes of drugs, the iMIDs, proteasome inhibitors, steroids, and standard chemotherapy make up the vast majority of the effective FDA-approved therapies for myeloma.