



Why Bisphosphonates Are an Important Tool in Myeloma Treatment

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Jack Aiello:

Can you also talk about bisphosphonates, pamidronate (Aredia) and zoledronic acid (Zometa) and the benefits, and how long should we be on bisphosphonates, if at all?

Dr. Orlowski:

Great question. We talked earlier about the fact that myeloma does affect the bone. And for people who have bone disease due to myeloma, bisphosphonates are often recommended. One of the drugs is called zoledronic acid. And there are others in this category. The benefit of them is that we know they reduce the risk of new fractures from occurring. They help to preserve the bone density. And there was actually one large study done in England that suggested that they may actually help patients live longer. Maybe they have some anti-myeloma effect.

The main issues to keep in mind with this class of drugs is that before you start on them, first of all, you should have a good dental exam, because there is a risk of something called jaw osteonecrosis. It doesn't happen often, but you want to make sure you don't have any, for example, abscesses or bad cavities before you start on them.

And you should have your urine monitored for any increase in the amount of protein that's coming out because that can be a sign of kidney damage in the future from these drugs. In terms of the duration, there are different recommendations. And right now, probably either 18 or 24 months is what's used most commonly. But we do need more data in this area, because my personal feeling is that we probably overtreat with these drugs compared to what we need, especially since some of the chemotherapy combinations are so active now. The main thing you want to do to preserve your bones is to kill off as many myeloma cells as possible.

Dr. Richardson:

I would say that I do agree with Bob that bisphosphonates are an extremely important part of the armamentarium. The way I kind of look at them in a metaphorical sense is you kind of have the Army, the Navy, and the Air Force of your main treatments. And then bisphosphonates, to me, are a sort of Coast Guard.

They keep bone disease to a dull roar. And they're very, very important, because Bob touched on the British trial, which showed survival benefit to bisphosphonates. And I think it's not trivial. This was a study of 2,000 patients. It was a comparison of zoledronic acid in one arm versus an oral, less effective bisphosphonate in the other. And the survival benefit was not small. The median difference was six months. To me, that's a very important piece of data, because it tells you that there is more than just this effect on the bone neighborhood that matters.

And we have compelling evidence from other trials that bisphosphonates not only reduce the time to bony events but may interestingly enough also fascinatingly have some immunological effects, which might explain some of the provocative data in smoldering myeloma where some evidence of clinical benefit to bisphosphonate use was seen. I do agree with Bob though that like any medicine that works, you have to be vigilant about side effects. The good news is that osteonecrosis of the jaw, which was thought to be a really terrible problem when it first emerged, has been understood now to be rare, as Bob points out.

And with the appropriate dental hygiene and management, it's actually relatively uncommon. For example, in the British trial, the incidents of osteonecrosis of the jaw was just 3.5 percent. And certainly, in our own group, we work very closely with our oral medicine colleagues and find this to be a very manageable issue now, whereas, in the past, of course, it was much more difficult. I do agree with Bob. We have to be careful about renal function with bisphosphonates, particularly with zoledronic acid. Pamidronic acid, which is Aredia, appears to be less of a challenge from a renal point of view.

And I think Bob touches on a critical point. How long should you use bisphosphonates for? And I agree with Bob that the duration of therapy for two years from diagnosis administered on a monthly basis is a relative standard. Beyond that, it's not clear. Should it be every three months? Should it be every six months? We don't know.

Certainly, every three months appears to be a minimum. And for patients who are not in complete remission and have active bone disease, clearly stopping at two years and not going back to bisphosphonates doesn't make sense, because, in reality, the effect of a bisphosphonate is not, for example, when it sits in the cortical bone. It's the journey of the bisphosphonate from the bloodstream into the bone is where its therapeutic effect lies, which is at the interface of where bone-forming agents and bone-destroying agents, or rather cells, osteoclasts and osteoblasts, sit. So it's important to understand that concept.

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