Dr. Michael Mauro: An Expert Answers Your CML Questions

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Andrew Schorr:
Hello. I'm Andrew Schorr from Patient Power, and we appreciate the questions you send us in from the CML community. Joining me now from New York is a noted CML expert, Dr. Michael Mauro, at Memorial Sloan Kettering Cancer Institute. Thanks for being with us, Dr. Mauro.

Dr. Mauro:
Thanks for having me, Andrew.

Andrew Schorr:
We got a bunch of questions from the community, and I just want to pose them to you. Dr. Mauro, you spoke about learning how to maybe reduce the dose in a given medicine and reduce side effects and still be effective, and we have many, many people who are taking TKIs. Where are we now with a couple things? One is being able to be mindful and control or reduce side effects, and the other is the worry that some patients have. If I'm taking these medicines for a long time, is it affecting some system in my body, whether it's my heart or my digestion, which is going to give me long-term problems?

Dr. Mauro:
Those are great questions, Andrew. I think you know how important it is when you see in the education session, which is designed to teach us all as hematologists what we ought to be on sort of the basic nuts and bolts, is that we had a cardio-oncologist give one of the CML education sessions from outlining cardiovascular toxicity from TKIs, so that's becoming a very important subject, and I encourage people to become aware of really just the basics.

The problem is that when someone may have CML their other health issues may be deemphasized or may not be followed as closely, and we actually need to do the opposite and make sure we know full well of someone's comorbidities and their other health issues, particularly cardiovascular health. And at the moment, we have some basic recommendations which aren't too far off what we ought to be doing anyway irrespective of the CML, meaning control your blood pressure and make sure you monitor it to make sure hypertension doesn't develop. Keep an eye on blood sugar lipids, have stress testing done, essentially what we should be doing for all patients.

As far as TKIs go, certain drugs are going to have greater risks than others, and there may be specific things we need to do for certain drugs, and we need to understand the mechanism of why some patients seem to have more complications in the cardiovascular space than others, or certain drugs have more risks than others, and that's still in development. For the time being I would propose sort of a blanket statement that pay attention to cardiovascular health, particularly if you're on

drugs with somewhat higher risk. Nilotinib (Tasigna) and ponatinib (Iclusig) are the drugs that seem to have a bit more risk. And with that alone we ought to be making improvement.

Some of the other questions we've had have been I think reassuringly dismissed. We don't see a lot of other long-term tolerability or toxicity issues. Some of the subtle things that can develop might be changes in cardiopulmonary status, pulmonary hypertension may be seen with dasatinib (Sprycel). That's something to be on the lookout for. Pleural effusions can develop late in with dasatinib therapy even years into treatment, so that's something to be always mindful of.

But what people are really worried about is is long-term care treatment going to jeopardize my health? I think the only subtle thing might be that some patients have a subtle decline in renal function or kidney function perhaps with imatinib, particularly in the elderly, Gleevec that is. And bosutinib may have a similar pattern. So good general internal medicine follow-up should answer these questions, but there aren't any big roadblocks, except for this cardiovascular question that we need to jump in order to feel comfortable still with chronic long-term therapy for CML.

Andrew Schorr:
Two other questions we got in from our community. One is about combining therapies. Now, obviously these are expensive medicines, but people know in cancer often medicines are combined for sort of a bigger bang, if you will. Is that something now in CML, or where do we stand with that?

Dr. Mauro:
Sure. It wasn't at this year's ASH but in the previous meetings a new drug called ABL's, year one, has come onto the scene. And what's interesting about that drug is it's—now it's a fourth-generation of ABL kinase inhibitors, but what's unique about it is it's the first drug we can combine with the drugs we have available because it's treating the leukemia by blocking these on a different site that no other drugs work.

Combining the drugs we have together doesn't really make sense because you're trying to shoot two arrows at the same bull's eye, and that's not going to really probably be beneficial. That's why we've never seen combination TKI therapies. But combinations now with ABL zero or year one I think are going to be emerging. We have very nice data that that drug works for people with multidrug resistance and intolerance issues with several TKIs as a single agent, and that seems to be safe to combine with imatinib and nilotinib and dasatinib. So stay tuned for further information about that.

The other thing that's happening is we're borrowing medications from other areas that might have efficacy in CML, particularly with low-volume CML, maybe to allow patients to deepen their remission or potentially make it more feasible to come off their drug. I think some of the encouraging data comes from a variety of different areas. One example might be ruxolitinib (Jakafi), the drug we use in myelofibrosis polycythemia, probable has a role in pH-positive disease as well. And there's some nice early data with combining that with nilotinib that it may deepen response, and there's trials being launched to look at that further, both to improve response and to perhaps make treatment-free remission more feasible.

There's a small company with a great drug called inecalcitol, which is a vitamin D analog, which has been shown to combine with Gleevec and deepen responses, and that's another thing that might be suitable to allow more patients to come off treatment ultimately based on this early data that it can deepen response when you combine it with TKIs.

And then the list grows from there. There's information about the older diabetes drug, pioglitazone, based on its effect on CML stem cells, and there are trials in France and the U.S. collaboratively and elsewhere looking at that. There are other ideas that you see in the literature, antibiotics and a number of different things that potentially have roles at the stem cell level.

So I think it's an exciting time that we're looking at hopefully drugs with low side effect profiles that might be intriguing or may not be obvious but could really do even better than we're doing now when it comes to getting high-quality remissions or maybe getting to treatment-free remission.

Andrew Schorr:

One last thing is one of our community members wrote in, and this is something you hear across cancer, and say, well, is there some help I can get for the fatigue I'm feeling, which some people get with these medicines or with the underlying condition. What do you say about that?

Dr. Mauro:
That's a tough one. It's been an under researched question because I think we've done so well in CML with targeted therapy that we just now are really making sure we're covering all the bases with regards to even subtle, chronic, low-grade adverse effects like fatigue, and I think as we understand it better—the first bit of advice is to make sure we're not missing a co—common problem.

For example, people on thyroid replacement may need more of it if they're on a TKI because of an interaction between the way the thyroid hormone is carried in the blood. That's—would be fairly obvious, but can be the case in some people. Anemia, of course. But I think there's still research to be done as to why the drugs cause fatigue. It immediately drive us to think about dose optimization. Probably forces us to think about how feasible and how practical treatment-free remission is because if it's something we can't work around certainly more manageable to think about a defined-duration treatment than something that seems forever.

And we have some cognitive research that's going on, too, to look at fatigue and maybe forgetfulness or the fog people feel like they're in with chemotherapy that's now blossoming in CML. That will be hopefully fruitful to give us some idea. But for all the good there's still some bad that has to be kind of tweaked, and that's probably one area that's still ripe for development.

Andrew Schorr:
So, Dr. Mauro, I've known you for years so I always like to wrap up with this: You are so devoted to this, you're a subspecialist in this area for many years. For people maybe newly diagnosed or people living a long time, how encouraged are you that with everything you've described we're getting a handle on the management of CML better than ever before?

Dr. Mauro:
I would absolutely echo that. I—I'm delighted to go to my clinic where now sometimes I have folks that have been off treatment for a number of months or longer. I have the ability to talk to people about the kind of ideas we just reviewed, and we still have new drugs in development like ABL one, where I had patients with very little options who—we turned things completely around and they look like they had a fresh start on a new TKI and went into a deep remission, so and I think we can finish—close the loop on some of the side effects issues we have and safely proceed in this era of treatment-free remission. We're really going have an even better end to the story than we have now, which is that—the thing I like to open up a discussion with a new patient is that CML fortunately in 2017, 2018 is now a highly treatable, hopefully functionally curable form of leukemia with an oral outpatient-based treatment, and that's remarkable.

Andrew Schorr:
That is great, great continuing news. Dr. Michael Mauro from Memorial Sloan Kettering in New York, thanks for being with us and answering questions from the CML community.

Dr. Mauro:
Oh, my pleasure. No question is unimportant.

Andrew Schorr:
Okay. And we look for your questions any time. Just send them to CML at patientpower.info. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.