Updates From ASH 2018: The Latest on Interferon Therapy in MPNs

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Andrew Schorr:
Hello and welcome to Patient Power. I'm Andrew Schorr. We've got two top MPN experts with me. We've cornered them at the American Society of Hematology meeting where they all come from around the world and around the country. We have Dr. Yacoub with us from the University of Kansas. Thank you. And we have Dr. Verstovsek with us from the MD Anderson Cancer Center Houston. We're talking about the role of interferon, particularly for patients with ET and PV, sometimes for MF. Where does it come into play and what are we hearing about it now?

So let's start with you first, Dr. Yacoub. So you have a lot of patients where you use interferon. So what's its role? And what about formulations of interferon that are helping you maybe do better with it too?

Dr. Yacoub:
Correct. So interferon is a naturally occurring hormone the body makes to boost the immune system and get some immune functions to happen by fighting infections like influenza. So these are molecules that do exist in nature, and we've learned as blood doctors to use them for decades now for treating cancers and leukemia and also myeloproliferative neoplasms. And the recent advances in the last 20 years or so is that we have a chemically modified version of it. It's pegylated. You add some sugar molecules to the interferon so that you can administer it less often, and you have a lot less side effects.

So the modern era of interferon use is a lot more safe and more effective, and we're using it a lot more at different stages of the diseases, early on or later on or in combinations at this time.

Andrew Schorr:
And what's the benefit over some of the older drugs you have had, let's say, for ET or PV?

Dr. Yacoub:
So in terms of activity we're still doing a lot of clinical trials to find out what is the drug that is more active. It's—we have—there's a lot of active research to try to better define what is the right way to treat patients and which drug to start with, and that still is an ongoing debate, and there's a lot of active clinical trials in that sense.

Interferons have a remarkable safety profile in terms of long-term use and the lack of cancer-forming risk that you can have with other drugs. So interferons can be used in young individuals who unfortunately need treatment for MPNs. They are safe during pregnancy. They are not associated with decreased fertility. So these are drugs that can be used safely at different stages of life that you can't use chemotherapy or other molecules for.

Andrew Schorr:
Like hydroxyurea (Hydrea).

Dr. Yacoub:
Like hydroxyurea.

Dr. Verstovsek:
And we all know, and we believe that there's a potential for interferon to change the biology of the disease in terms of decreasing or eliminating cells that have mutations, perhaps improving the bone marrow function, normalizing the bone marrow. That is being studied. It is not the goal for the therapy to aim for the molecular response or the bone marrow response. The goal of therapy still is to decrease and normalize the blood count to eliminate or decrease the risk of thrombosis, but these medications may have long-term implications, right?

Dr. Yacoub:
Correct. Yes. So that's a very important point. So our goals of care remain the same. We want patients to feel well. We want them to be protected from their cancer complications, which are clotting and bleeding and other symptoms of the disease. So when we compare hydroxyurea to interferons, let's say in the clinical trials we're doing right now, but there's also this premise that interferons will be a long-term investment where you're putting a high-impact intervention early in the disease course that many years or decades later will be disease-modifying and even achieving deep responses of remission, and even beyond that there's now treatment-free remission where patients are off therapy and they have no symptoms of their disease. So we're getting at that end of the spectrum, the era after you have no therapy and no disease that is symptomatic.

Dr. Verstovsek:
We upped our attempt from normalization of the blood cell count to a higher grade or a better grade of response, disease modification leading to perhaps disease elimination. The implications are maybe you don't need to treat anymore forever. We are exploring that with interferons.

Andrew Schorr:
Right. So let's talk about that for a minute. So there are new formulations that are developed, some used in Europe, and you've been testing here. Where are we now with kind of new versions of interferon?

Dr. Verstovsek:
So one of these long-acting interferons which we know about and it's being tested in a number of clinical studies is called Pegasys, United States and in Europe, compared to hydroxyurea like you just described. But there is another one I like. It's called super long-acting. You know, Pegasus has this pegylated part that makes it long acting for a week, we give it weekly. The super long-acting, which is called ropeginterferon, or ropeg for short and is given every two weeks and perhaps even once a month. So if there is any side effect, it would not be obvious because side effects are usually related to injections. You have those flu-like symptoms. And you can then deliver, right?

And then delivery of the medication a safe way would deliver that possible biological effect not only on control of the blood cell count, which is high, but also increasing what while were saying, the JAK2 number of cells, JAK2 allele burden, perhaps including the bone marrow, but the JAK2 allele burden would be indication of the biological modification. So implications are beyond just thrombotic.

Dr. Yacoub:
Correct.

Andrew Schorr:
Okay. So this is a discussion that someone might have with their MPN specialist is—for PV and for ET for sure—is does interferon or maybe a trial even related to longer or longer-acting interferon, does that work for me, right?

Dr. Yacoub:
So it has been studied at different stages of myeloproliferative neoplasms. We seem to think it's going to be active in essential thrombocytopenia and polycythemia vera, and in the very early phases of myelofibrosis. So some activity, biological activity are observed when you can interfere early in the natural course of the disease, but a lot of times when it's--when the disease has evolved beyond the phase where interferon can work it is not active like in advance myelofibrosis, for example.

Andrew Schorr:
Okay. But if it hasn't advanced would interferon—we've been looking at combinations and you and I have spoken about it—would interferon ever be combine with like ruxolitinib (Jakafi)?

Dr. Yacoub:
So there is a presentation in this meeting, but I think the results are not yet mature enough to give us the right signal. So the use of interferon, they are very active drugs, they are very promising, but they do come in with side effects, and certain toxicities, some of them are serious. So the use of interferon should be with a physician that has experience and comfort level managing the side effects of the therapy. So to do that, to combine them has to be under a clinical trial setting. I would not recommend that to be performed without that level of supervision.

Dr. Verstovsek:
I absolutely agree. And in case of the ropeginterferon there are three studies or results of three studies that are being presented here. All these studies unfortunately, or fortunately for patients that can access it in Europe, not done in the United States as of yet. It was a study in long-term outcome patients in the—with ropeginterferon treated that have a PV, then as you said in early-stage myelofibrosis, prefibrotic myelofibrosis and the last study which is actually oral presentation here is comparison to Hydrea where it appears to be better than hydroxyurea in polycythemia vera.

So all these studies talk about the efficacy of this medication. Hopefully, we will have it in clinical studies, and I encourage everybody to participate, in ET and possibly in PV here in the United States.

Andrew Schorr:
Okay. But for our worldwide audience it may be in Europe that it's accessible.

Dr. Verstovsek:
In Europe it's being done, not in the United States. I'm not aware of any other countries.

Andrew Schorr:
Okay. And just so I understand. You alluded to side effects. Just to be clear, with these interferons what are the side effect? Sometimes flu-like symptoms. What else would you mention?

Dr. Verstovsek:
Sometimes autoimmune problems. It can affect the body functions in general. That means the body can be affected by some problems with the thyroid functions or the liver functions or kidney--

Andrew Schorr:
That has to be monitored.

Dr. Verstovsek:
That needs to be monitored. So for new medications, although highly promising like ropeginterferon, one is to have very well designed clinical studies, select patients that would be exposed to the drug because it's necessary with defined goals and with the safety monitoring in place.

Dr. Yacoub:
Correct. So among the very important side effects that we highlight and usually they are a reason to not use interferon would be patients with autoimmune diseases and also patients with out-of-control depression.

Dr. Verstovsek:
Correct.

Dr. Yacoub:
So these are conditions where interferon use is probably not wise, so choosing the right patient for the right treatment is important. But with those exceptions interferon compared to hydroxyurea, whether in the first-line setting or the second-line setting, has shown that it is a very active molecule that is equally active to the other drugs and the side effects are not worse. So hydroxyurea does have side effects as well as interferon does.

Andrew Schorr:
But it may have benefits.

Dr. Yacoub:
Yes, and in a very thorough evaluation of patients' quality of life interferon use is not associated with worsening quality of life. It is as good as therapy with hydroxyurea. So I know there's a perceived notion that interferon use is associated with intolerable side effects by even some experts in the field, but in a prospective fashion, in a clinical trial, this was not proven or found to be true.

Andrew Schorr:
Okay. So it's a matter of what are the facts, and the data continues to come out in this. And as you said there are studies being presented at this ASH meeting as we recorded. So that's a discussion if you're living with one of these conditions. Does some formulation of interferon apply to you? Is there a trial that may open up that you might want to be part of to see whether this naturally occurring substance may be right for you versus something else, some hydroxyurea and other drugs you have had that could have—might not be right in certain times of your life like talked about, pregnancy or at certain points or might have some down-the-road worries, right? Did I get it right?

Dr. Yacoub:
Correct.

Andrew Schorr:
Okay. Dr. Yacoub from the University of Kansas, thank you for being with us.

Dr. Yacoub:
Thank you very much.

Andrew Schorr:
And Serge Verstovsek from MD Anderson.

Dr. Verstovsek:
Thank you so much.

Andrew Schorr:
Thank you for being with us. Okay. Hopefully this informs you more about interferon, and we'll continue to follow it in our programs. Send us questions to questions@patientpower.info.

I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.

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