Understanding Placebo Groups in Clinical Trials

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Ellen:
Yes, I'm a patient. I'm in the watch and wait.

Andrew Schorr:
And your name?

Ellen:
Ellen.

Andrew Schorr:
Okay, Ellen, what's your question?

Ellen:
When you talked about clinical trials, you never mentioned a placebo group, and are you still using the placebo groups for clinical trials?

Andrew Schorr:
Right. And just so everybody understands, so let's say you get excited about being in a trial, you're worried are you getting what could be that hot, new medicine that they're studying. So that would be a question. So do you want to talk about that, Dr. Munoz? Because that would be my fear is I'm not getting the good stuff, you know?

Dr. Munoz:
Absolutely. We all understand that fear. It is human nature to think that way. But more and more, we try to shy away from placebo or sugar pills. For example, the study that showed us the good results that idelalisib (Zydelig®) brought, it was idelalisib plus rituximab compared rituximab (Rituxan®) plus placebo.

So yes, there are studies that can have placebo. But it does not mean that you will not get any sort of treatment when you enroll in the drug. You usually will get an active drug. But you may or may not get the novel agent. We still strongly encourage our patients to enroll in one of these clinical trials, because they say that drug development takes 10 years or so to bring one drug from Phase I to Phase II to Phase III and to the clinic. So if you enroll in the clinical trial, you can fast-forward. You can jump ahead 10 years, in theory, and get the drug from the future now.

Andrew Schorr:
Dr. Jain, so there's a trial design called a crossover study. Could you explain that where you may be switched if you were on the placebo side, you may be switched?

Dr. Jain:
So I think just to kind of carry on that conversation, so this concept of placebo generally comes into play in Phase III randomized clinical trials. So if you are on a Phase I or Phase II, you will be very likely getting the drug.

And you will be told that this is the drug you are getting. When you reach Phase III, which is a randomized clinical trial, so generally, in the medical community, there is a concept called equipoise meaning that if we have two arms to the study, I, as a clinician or an investigator, feel that either of the arms is equal. I don't know which is better. And that is why I want to do the clinical trial. So even if there is a placebo, it will be with something. It won't be that you're just getting placebo for your CLL and nothing else. So as Dr. Munoz said, in one of the major studies, which led to the idelalisib approval, the idelalisib was combined with rituximab.

And the other arm just got rituximab. So they still got just rituximab but with placebo. Now, the crossover means that once—in that particular story, the crossover was a lot later. So once you progress, then, if you are on the placebo arm, when you progress, they will blind the randomization, meaning that then the clinician knows that actually what you got.

And if you are on the placebo arm, you have the option of getting the active drug. So let's suppose six months down the line, you're starting on the treatment. And then you progressed. Then you have the ability to cross over to the active drug arm. So that is something we also look for our patients, and we encourage clinical trials development. Most of the Phase III trials are generally led by drug companies. So in discussions with them, we encourage them to involve a crossover so that the patients, all patients potentially, then will benefit from the active drug.

Dr. Ferrajoli:
You will never be receiving placebo without you knowing. Every time you sign up for a clinical trial, they will explain. You will have very detailed explanation of what is that will happen to you. So just by clinical research ethics, we are prohibited from telling you that you will be receiving a medication and instead giving you nothing.

So everything that you receive and you sign up for will be exactly how it's written. This is highly, highly regulated from ethical and legal point of view.