Transcript | Your CLL Questions Answered

Michele Nadeem-Baker:
Welcome back to *Patient Power CLL Town Hall*. I'm Michele Nadeem-Baker and joining me on this particular segment is Andrew Schorr. Hi, Andrew.

Andrew Schorr:
I wanted to just make a couple of points before we go through massive Q & A with our doctors, and that is help people. I know we have some newly-diagnosed people. So look; the different classes of medicines that we are blessed with having now. BTK inhibitors, that stands for Bruton's tyrosine kinase inhibitors. There are two approved ones, ibrutinib (Imbruvica) and acalabrutinib (Calquence). One probably near-pending approval, zanubrutinib (Brukinsa). There are others. There's a new generation that's in trials, and that may come up. There is the Bcl-2 inhibitor, a different class of medicine, venetoclax (Venclexta).

And there is another approach we've been talking about, monoclonal antibody. Some people over the years have had rituximab (Rituxan). That's a monoclonal antibody, more recently, obinutuzumab (Gazyva). So that's what a lot of the talk is. We've got some great questions. So let's get our doctors on. Doctors, are you ready to go?

Dr. Furman:
Absolutely.

Andrew Schorr:
Okay. Here we go.

Michele Nadeem-Baker:
We certainly have a lot of questions, and also, some that we have from our last programs that haven't been answered as well.

Andrew Schorr:
Yeah. Dr. Furman, we have thousands of people who are on the original BTK inhibitor, ibrutinib. So they want to know, "If I'm doing okay, despite these combos or other newer BTKs, should I switch? Or is it, if it's not broken, don't fix it?" How do you view it?

Dr. Furman:
So I am a little superstitious. And I do believe, if it's not broken, don't fix it. But I do also have an eye towards those adverse events that do look like they're long-term risks of ibrutinib, mainly, the hypertension and the atrial fibrillation. So if I do have someone that is developing hypertension or has hypertension and it's worsening, I would, at that point in time, consider using one of the other BTK inhibitors, primarily because I want to limit their side effects or worsening the comorbidities. I don't really go for accommodation or anything like that because this is someone who's doing really well on just a single-agent BTK inhibitor, and I would just continue with that.

Michele Nadeem-Baker:
Dr. Allan. We have someone in our audience – we've been talking about all these different combinations, and they were treated with rituximab and bendamustine (Bendeka and Treanda)

four years ago. They are wondering if that means that they would not be able to take obinutuzumab in a combination in the next treatment.

Dr. Allan:
It's a good question. The trials that studied these drugs, particularly venetoclax, in the relapsed setting after a prior therapy – let's say, bendamustine – that study did use rituximab, and it's approved in that setting. With that said, there's nothing necessarily special about venetoclax and rituximab in the relapsed/refractory setting. And frankly, in my practice, I do utilize obinutuzumab. We have a lot of evidence that shows that obinutuzumab might be a better antibody, particularly in the frontline setting, comparatively to rituximab, which is where, usually, obinutuzumab is being used. And so there's nothing that prevents your physician from utilizing obinutuzumab in a relapse setting. Commonly, myself, and in our practice, we will utilize obinutuzumab in relapse settings, "off-label" in these kinds of combinations, and usually, you can get insurance approved for it.

We know the toxicities of these drugs. Does it necessarily, in this setting, in the relapse setting, prove to be more beneficial over rituximab? We've never really shown *that*. Because all of the studies that have shown obinutuzumab to be better than rituximab have always been in a frontline setting, and so we extrapolate this data. But I talk to colleagues across the country; some are very by the book. And this is what the trial showed, and this is what they did the study with, and they use rituximab in the relapse setting.

Other physicians are like myself, to where we may extrapolate this frontline data to say, hey, this might be a better antibody, and we use it in a relapse setting. Obinutuzumab may have a slightly different toxicity profile. So it's not necessarily ideal for every single patient particularly, but it can be used. And just because you got rituximab frontline doesn't mean you can't use it in the relapse setting.

Andrew Schorr:
Okay. Dr. Furman. So, one of the choices we were talking about is time-limited therapy or fixed-duration. And so patients want to know what testing you do, whether it's this minimal or measurable residual disease testing, some kind of scan. What testing do you do to say, "Okay, we can stop."

Dr. Furman:
So it's important to remember that the data generated for the fixed-duration therapies are actually not MRD-guided. Currently, there's no evidence clinically to use MRD to make a therapeutic decision. So the fixed-duration therapies are all meant to be used for that duration of therapy. The continuous, they're meant to be used continuously. And so those are the data that we have.

Dr. Allan's study is unique in that it's using MRD to guide therapy. And that's sort of a unique approach, and we have many other clinical trials that are currently looking at that. But right now the idea is that, if you're doing obinutuzumab and venetoclax, it's supposed to be 12 months of therapy. If you're doing acalabrutinib, that's a single agent, you're supposed to be on it until you show evidence of disease progression. That's currently the way the medicines are meant to be prescribed.

Michele Nadeem-Baker:
Dr. Allan. What defines a CLL specialist? And I often see this a lot in the different support

groups that the patients are in. This person said their hematologist/oncologist is affiliated with an academic institution but isn't listed as a CLL specialist. And her credentials appear to be the same as the CLL specialist that she's viewed. What's the difference? This is a great question.

Dr. Allan:
There's really nothing special that makes Rick or I a specialist over other oncologists in the academic world. It's just that we have had an opportunity to focus most of our research, in the clinical trials in our institution, on CLL-specific research. And so lymphoma physicians, whether you're a CLL expert or not, may have many CLL patients. And are staying up-to-date on all of that data, participate in these clinical trials, and you're going to be in very, very good hands.

I think it comes down to experience. It comes down to is someone's specific research in that CLL space. Sometimes, a lymphoma doctor may be doing a lot of diffuse large B-cell lymphoma research but have a handful of patients with CLL. But it's just a relatively arbitrary term that we impart upon ourselves, and that we have this title. And it's mainly based on the fact that our research, what we run clinical trials on, is focused on patients with CLL. And in doing so, we attract CLL patients, where Dr. Furman's practice is probably close to 90% of patients with CLL. Mine, as it's growing, is now close to 60% of the patients that I see have CLL. The other patients have lymphoma. So we have expertise outside of CLL, even, but our practice is focused on developing trials, and studies, and using these targeted therapies, particularly in patients with CLL. And that's really the difference, I guess.

Andrew Schorr:
I just want to make a comment on that. So when a patient in the hinterland, though, wants to get a second opinion, something like that, there are lists. The CLL Society has them. Many of the top CLL specialists have been on our programs like this one. Dr. Furman's been on many times, Dr. Allan, others. I would say, "Go for the gusto (laughs)," so that you know the full range, the most trials, the broadest experience. That's not to denigrate other doctors where it's part of their practice. But if you do seek that out, we can easily get you the names and they're broadly available.

Dr. Furman. So I have a question for you. We mentioned along the way – Dr. Allan said, "Well, many of the CLL patients are 70 or older." Here's a question from someone who's 75 and they've been in watch and wait for 20 years. So they want to know, "I'm being monitored. I have labs every six months. Does each year that I'm in watch and wait increase the chance that I will never need treatment?"

Dr. Furman:
I mean that almost becomes a teleological question, right? And I think that it's – the idea that I'm a big believer that past behavior is a good predictor of future behavior. And so, yes. The longer that you remain stable, the longer you're going to remain stable. And it's interesting because we also teach or state that the median age of CLL, as it's increasing, as the population ages, the majority of these patients who are older do actually have more indolent courses.

But there are many, many younger patients, as this person demonstrates, who have had a very nice indolent course. And so that speaks to the variability that we had talked about earlier in CLL, and how we never know what the future holds, and that's the important thing. So I am a believer that past behavior is a good predictor of future behavior, and each year additionally, just bodes better.

Michele Nadeem-Baker:
Dr. Allan. We were talking about clinical trials earlier in our program, and also, in our first segment, about cost and how prohibitive costs can be to patients. Are clinical trials provided at no cost to the patient?

Dr. Allan:
Yes and no. Certain features are going to be covered by the study. So, a trial – and as investigators who open these studies, we are tasked with assigning whether a procedure, or a scan, or a lab test, or a study visit is considered standard of care or not. And if we state that we think it's a standard of care test, then that typically will go to insurance, your commercial insurance. If we think a scan, after the first six months of treatment, is standard of care, which typically it is, because we always need a scan to assess a true response, we may send that scan to your insurance.

Now if the study requires a scan three months later, I would frequently say that is a research study. That is for this study only, and if you weren't on this protocol, you would not be getting this. That is where the budgeting and the contracting, that we do all behind the scenes before we even open a study, goes on. And there are negotiations with the payers and the sponsors, etc., to fund that study. Now that scan would be paid for by the study. It would not go to your insurance.

So typically, the drugs that are involved and being provided are free of charge, but there are going to be standard-of-care costs. So if you have a co-insurance, let's say, that you will have to pay up to $2000, because your co-insurance requires you to pay $2000, or a $500 deductible, or whatever it might be. You will have to pay that, in terms of the standard-of-care labs, or scans, and things like that, and you will potentially get a bill for that until you meet that deductible or co-insurance.

And so there are times when patients get confused. They're on a study, that they think it's just everything is going to be covered. But they flip into a new year, and all of a sudden, that scan is January 4th, let's say, and all of a sudden, your new deductible and co-insurance now sets in. For that scan, you might have to pay the $500 deductible all of a sudden, when previously, all of the other scans were free, and it can be confusing. And so we get these calls. That's where the research team and the nurses help you understand what your out-of-pocket cost may be, and explanations of these benefits from your company.

So, yes and no. There are many things that are covered in the clinical trial space, but there are also many things that are being put into your insurance that are standard of care. Because that is just part of taking care of you, whether or not you're on a study or not.

Michele Nadeem-Baker:
I know personally, myself, I thought "clinical trial," in the beginning, I was under the misconception that that that means you don't pay for anything. And then the bills started coming, and I was like, "They must not have been submitted correctly by my institution," but in fact, they were. So thank you.

Andrew Schorr:
Get stuff done in December and not January.

Michele Nadeem-Baker:
Exactly.

Andrew Schorr:
Anyway, Dr. Furman. Earlier we had a patient on who was in a trial, and she had had Richter's transformation. So the questions come up from the audience. What is Richter's transformation, and is that another "shoe" that we have to worry about dropping if we have CLL?

Dr. Furman:
So Richter's transformation – basically, it's when CLL, which is a low-grade lymphoma, becomes an aggressive lymphoma. And it's most commonly going to be what should be thought of as a diffuse large B-cell lymphoma, but it may also be a Hodgkin's disease. And these are aggressive lymphomas that are treated with standard cytotoxic chemotherapies. And unfortunately, because CLL patients who transform often have a lot of bad characteristics, are often difficult to treat. The transformations are often difficult to treat also, because usually the bone marrow is impacted with CLL, or because of prior chemoimmunotherapy, is not as healthy. And that sort of impairs our ability to treat the now aggressive lymphoma that's present.

The thing that I think that's most important to keep in mind is, we've really developed a great number of ways of identifying, ahead of time, who are the people likely to develop Richter's transformations. And from the data that we have, there are certain genetic abnormalities that are at risk. But I think what's most important is that it is a biological phenomenon, that's related to either the inherent biology of the cell and therefore, it's going to happen typically within the first couple of years of diagnosis. Or that it's going to be the result of chemoimmunotherapy and 17p deletion which results from the chemoimmunotherapy.

So my hope is, obviously, with the chemoimmunotherapy no longer being used, Richter's will become less prevalent and less of an issue. I do believe that as long as CLL stays CLL, we will be able to take care of that patient and keep that patient well. That transformation does have an impact on how that goes overall.

Andrew Schorr:
Should we lose sleep over it?

Dr. Furman:
Well, I think overall, that it's probably going to be less than 10% of patients that do develop Richter's transformations. And if you don't have any of the worrisome features, and if you're beyond that two-year mark, you're free and clear and in great shape. If you're within that two-year mark, I mean, the risks are still incredibly small, and I wouldn't lose sleep on it. Because the truth is, is that there are things that are being developed all the time that will certainly help, even take care of Richter's transformation.

Dr. Allan:
Yeah. I'd like to just plug one thing there too, talking about these new developments. We do have a study here, for Richter's transformation in patients who've had CLL that have had this transformation event. Adding a drug called polatuzumab (Polivy) to the standard-of-care chemo backbone, like CHOP-like treatment. In this case, it's EPOCH (etoposide, prednisone, vincristine sulphate, cyclophosphamide, and doxorubicin). And so we do have that for treatment-naïve Richter's transformations. You could have had prior therapy for your CLL, but if the transformation event has not been prior treated, that study is potentially eligible for patients

there. And it's something that we are accruing at a few sites here in the New York area and is being led by our team here at Cornell, and we do have it currently open and accruing at our center right now.

Andrew Schorr:
Thank you. That could be great information for somebody facing that. Michele?

Michele Nadeem-Baker:
I'm going to mix things up here. I'm going to go to you, Dr. Furman.

Dr. Furman:
Okay.

Michele Nadeem-Baker:
What does high-risk watch and wait mean, and do you start treatment sooner? So we have so many patients who have been writing in that they have 17p, TP53, and they are told they are on a high-risk watch and wait. Can you explain what that would mean for someone?

Dr. Furman:
Sure, yeah. So one of the things that we do very poorly is define our terms in CLL, and this is a great example. "High-risk" is just a relative term. We have patients who are high-risk because they have unmutated immunoglobulin genes compared to mutated immunoglobulin genes. But the truth is, the high risk in that situation means that these are patients who are at risk of progressing. But we know that if you take unmutated immunoglobulin genes in CLL patients and give them a BTK inhibitor, they do equally well as the mutated CLL patients given the BTK inhibitor. So while it's high risk of progression, it's not high risk of responding and it's not high risk of having a bad outcome long-term.

So when we talk about what I believe to be truly high-risk watch and wait patients, it's those patients who are at high risk of either – the way I look at it is that 80% of CLL patients will be able to probably receive a single-agent BTK inhibitor and have a response that's indefinite. Twenty percent, though, are either going to be at risk of responding and then progressing, or developing a transformation, and these 20% are the people that I call at high-risk. And so the higher risk is going to be characterized by those people with certain mutations, like a TP53 mutation, or a 17p deletion, a NOTCH1 mutation, or certain stereotyped V-genes that predict for the CLL being able to escape single-agent BTK inhibitor therapy or transformed. And we actually have trials, particularly targeting these patients with a goal of trying to lessen the likelihood of this happening.

Andrew Schorr:
I have three quickies for you, Dr. Allan. The first is, is it true that CLL folks need to be extra proactive with sun exposure? And if so, how come?

Dr. Allan:
Yeah. So it's a great question. We know patients with CLL, as well as other indolent non-Hodgkin lymphomas, like follicular, and marginal zone, and other lymphomas, do have a higher risk of skin cancers, and particularly, in CLL. And most of the time, these are squamous cells or basal cells, which are a lower-risk type of cancer, frequently will stay in the one spot that they're at. But need to be dealt with, obviously, and we do know that there is an increased risk in our CLL patients. And mostly, that's likely from an immune dysregulation that is going on from the

CLL. Our T cells and our immune system are very good at surveilling for dysplastic and abnormal cells that are expressing proteins that they shouldn't, And that immune system is constantly surveilling and gobbling up these bad cells. And frequently, when you have CLL or some other lymphoma dysregulating that immune system, that surveillance can get out of whack.

And so we do see this incidence higher in our CLL patients. And so, therefore, I do always tell my patients: one, if they have a history of an abnormal lesion, even before they were diagnosed with CLL, let's say, to get back with your dermatologist. And if there's a history of an actual skin cancer, be seeing them, re-establish care, every six months essentially, for a total-body skin exam. If you haven't had a malignancy yet, but you may have had some abnormalities, then again, establishing care and getting that total-body skin exam at least once a year.

And then obviously, when you're out in the sun, to have proper sun hygiene, wearing hats, using sunscreen. And to remember this fact because it is something that we don't want to deal with. It can complicate care sometimes. BTK inhibitors have risks of bleeding. And if you need to have a Mohs surgery or some biopsy constantly, you may need to be coming on and off these treatments. And so prevention is going to go a long way at improving a long-term outcome, potentially, by keeping you on these drugs and not having complications from surgeries or procedures, and it just goes a long way at managing that.

Andrew Schorr:
One quick follow-up related to something else. Somebody wrote in and said, "I'm due for a colonoscopy. Are there any CLL treatments that should be discontinued before I have the procedure?"

Dr. Allan:
Yeah, it's a great question. This is another thing I always reiterate with my patients. Because patients are going to do so well, that it's really important to stay up with your mammograms, your colonoscopies, your cholesterol, your blood pressure, all of these things, and your routine cancer screening because we can deal with the CLL. We can manage that very long-term and you're going to have an outstanding outcome. But what we don't want to have happen is we ignore these other things, and a polyp turns into a colon cancer, and so on and so forth.

You never know what you might find in these biopsies or colonoscopies. If there is a polyp there, typically, just to have the procedure of a colonoscopy or an endoscopy, you don't need to hold the drug. The issue is where; if there is a need for a biopsy, or a snaring of a polyp, or some procedure that they need to get several biopsies, that's where there can be some increased bleeding. It's a low-risk procedure typically. I frequently, especially in patients who've been on drug for quite some time already, have no problem holding the drug for two to three days before the colonoscopy, in case that a biopsy needs to be done, and then re-starting it soon after if there are no bleeding complications.

For patients who are just starting out on treatment, I frequently ask that if they can postpone, and if it's just a screening type of colonoscopy, to maybe wait six months or so if you can to get the disease under control, so I'm not having to worry about holding the drug. But these are all opinions, and there are no real strong guidelines, honestly. And you could probably ask 10 different physicians and get 10 different answers about how do they manage a patient around a colonoscopy. In general, I try to minimize how long I have patients off of drug. But these can be procedures that bleed, prostate biopsies can bleed, and these can be complicated by these

agents that we are on. So frequently, colonoscopies, prostate biopsies, little Mohs surgeries, I am holding these drugs prior to it.

Michele Nadeem-Baker:
We have a question. Is it okay to be on and off ibrutinib or acalabrutinib, if you have to have a continuation of different things, such as steroid injections or say, Mohs surgery like you just said, and more things are found?

Dr. Allan:
Yeah. So for little, tiny injections, like knee steroid injections for arthritis and things along those lines into a joint – a thumb joint, wrist joint. I don't typically hold the drugs for these. And once you're talking about epidural-type of injections, and it's a little bit more high-price real estate, and it's going to be an elective surgery or procedure, I will typically favor to do it there. There's really no harm in these short holds in terms of the outcome. That we're not going to have some poor outcome because we hold the drug to ensure safety from some procedure for two to three days, or whatever it might be, or even a week.

So routine cleanings, that's another thing we get. I don't typically hold these drugs for routine cleanings. But if you are having dental implants, or you're pulling teeth, or there's anything that's going more intensive into the bone, that's where I will hold it. Because they can also be a bloody type of procedure, and we want to prevent that if we can.

Michele Nadeem-Baker:
Do you also suggest taking antibiotics prophylactically before a dental cleaning?

Dr. Allan:
For the CLL patients, a routine CLL patient that has no cardiac issues, I do not prophylax them. But obviously, whatever the guidelines are from their cardiologist; if they have a valve, or if they have aortic stenosis, or they have some replacement or cardiac indication for it, then obviously, you do. But that's more for the cardiac indication and they should discuss it with the cardiologist. But just because you have CLL, you do not need prophylaxis – or at least, I don't prophylax patients with antibiotics just for routine cleanings and things along those lines.

Michele Nadeem-Baker:
I'm sorry, one last follow-up. So someone has a steroid epidural one week, and they have to have their colonoscopy the next week or two weeks after. Is that okay to go on and off the drug, or do you need to space things apart more?

Dr. Allan:
No. I mean, it's okay to go on and off. But sometimes, if you can space it out, it's better to do that. Again, there's no great data about that. Sometimes if you have one procedure, and it's a minor procedure, like an injection, or something along those lines for a herniated disc. Sometimes to try to line them up, while you are off the drug for that one week and try to get everything done in that span of time. Otherwise, you can go on and off of these. It's less ideal to go on for three days and then just right off again and to maybe span it out to where you get more consistent suppression of the CLL before doing it.

Andrew Schorr:
Dr. Furman. I think Susan mentioned it earlier. But many people, particularly if they're in their 70s, have more than one condition going on, CLL, and this, and that. Now, one of our viewers

wrote in and said, "My fatigue is awful, but my counts are good. I'm on watch and wait. Can CLL be blamed on other issues, menopause, hormonal changes, or confused with CLL?" So when somebody says, "I'm tired, Dr. Furman." How do you sort it out, whether it's the CLL or something else?

Dr. Furman:
So this allows me to use one of my favorite expressions, which is, having CLL doesn't protect you from all the things that befuddle the rest of us, right?

Andrew Schorr:
(laughs)

Dr. Furman:
So common things occur commonly. The most common cause of fatigue in a patient with CLL is going to be the exact same – likely cause of fatigue in any individual. And the other data that someone actually once quoted was that 70% of CLL patients have fatigue, but 80% of New Yorkers have fatigue. It's so important to try to figure out whether or not this fatigue is truly CLL-related or not. So even if you have a high white count, if you don't have a lot of lymphadenopathy, anemia, or thrombocytopenia, or more importantly, if your disease isn't worsening, the likelihood of the fatigue being CLL-related is less so.

And it's always important to round up the usual suspects. Sleep apnea is incredibly undiagnosed. And just poor sleep hygiene, whether or not it's getting up because you have to urinate, or for whatever reason. And so, so often, treating these other conditions can resolve the fatigue, and the CLL is just a "red herring." So it is important; if someone is not showing frank signs of disease progression, I do try to exhaust all the other possible explanations for what we call those B symptoms.

Andrew Schorr:
And that's a great answer.

I just want to point out. Michele, you're hosting a program coming up that I just want people to be aware of in a couple of weeks, on time-limited therapy, with Dr. Jain from MD Anderson. And then my wife Esther and I are doing a program with Nicole Lamanna, also from New York City, about COVID and CLL. And so we probably should sneak in a question now, though, Michele, about COVID. Do you have one? Because you've been so careful.

Michele Nadeem-Baker:
I have been – yeah, the "poster girl" for being uber-careful. Maybe, perhaps, a little too careful, although I do venture out every now and then. I'm not totally just encased in here. So, as we know, CLL patients, should they contract COVID, it can affect us in a more severe way than someone who is not immunocompromised.

So my question for you, Dr. Allan, is, let's just say I get COVID and I'm on treatment. Here is a question from our audience. "Is my treatment affected if I do contract COVID?"

Dr. Allan:
Yes. So it's a great question. And it's a moving target, and there are probably a few ways to answer this question. So before we had treatments like Paxlovid (nirmatrelvir/ritonavir) and some of these antiviral therapies that are for our outpatients and those people who aren't with

severe COVID. These drugs, particularly Paxlovid, do have a companion agent in it that does affect the metabolism of our drugs, particularly our BTK inhibitors and our Bcl-2 inhibitors. They affect statins as well as blood thinners like Eliquis (apixaban). And so these agents, when you are prescribed this antiviral Paxlovid, do need to be stopped because they are strong CYP3A4 inhibitors and therefore can increase the levels of these agents that are for your CLL. They can increase the levels of the blood thinner with apixaban. So these drugs need to be stopped for the five-day course that you're on the remdesivir (Veklury). And once you're off of it, it washes out, and you can go back on your BTK inhibitors.

There is, probably, controversy out there regarding the effects of BTK inhibitors and anti-inflammatory properties in patients who are afflicted with COVID and severe COVID. We used to basically, not stop these drugs when patients developed COVID and left them on their BTK inhibitors. There is some anecdotal evidence that maybe, outcomes are improved. And much of this data is from the Delta era, where there was an overwhelming inflammatory response. There was thrombosis. There were all of these other factors. And there are rather impressive, eye-raising case reports of patients miraculously turning a corner once they re-started a BTK inhibitor if it was held. And since we've got such good drugs nowadays, these drugs, in general, BTK inhibitors, are immunosuppressive. We do see infections actually increase, or the risk of infections not be zero. And a third of patients have a significant infection in the first six months of starting these drugs, and this is before COVID. And so they are immunosuppressive agents. And in general, the teaching is, you stop these drugs when you have an infection.

And so this COVID flipped it on its head a little bit because of these other opportunities. In my practice, I am typically stopping these drugs now when patients get infected with COVID. Because I want their immune system to turn on naturally, particularly with Omicron, where it is a little less severe, particularly now that we have these antiviral agents like Paxlovid and other monoclonal antibodies. And particularly when we've got, now, prophylactic antibodies that might help neutralize the infection naturally. And therefore, the data is not strong enough for me to keep patients on these drugs, but it's controversial.

And again, if you line up 10 CLL physicians, they're going to have 10 different opinions about whether or not to continue these drugs on – in the absence of Paxlovid and some of these other agents, in a thought, to help prevent or ameliorate some of these COVID symptoms. And the data is not great, it's anecdotal. And ultimately, I've now gone to a practice, where I'm holding these drugs, let the patients get over their infection, and then talk about reintroduction upon improvement. And fortunately, in this Omicron area, the disease is much less severe. And we've got, now, outstanding treatments, that a lot of patients aren't even telling me they're getting infected anymore. They would come in and they'd tell me a month later, their primary care doctor's getting them Paxlovid. And they're not even letting us know nowadays, and that's how it's going for many patients.

Michele Nadeem-Baker:
So with those patients, they went off their BTK-is?

Dr. Allan:
Yes.

Michele Nadeem-Baker:
When they went on Paxlovid then?

Dr. Allan:
Yeah.

Michele Nadeem-Baker:
Even the ones who didn't tell you? Okay.

Dr. Allan:
Yes, you should go off of them. And that's also the danger, and why I always tell my patients to call us. Because if they are on treatment, the PCP doctors, and the primary care physicians, and the pulmonologists and things may not recognize that. And something that we intervene upon, and you hold the drug, and you take your medicine, and then you restart these things when you get back on.

Andrew Schorr:
Right.

Michele Nadeem-Baker:
Such an important-

Andrew Schorr:
Folks, communicate, communicate, communicate with the doctors that you trust. We have a whole program coming up on this. There are some replays, particularly, one recently with Susan O'Brien. I asked her specifically about Evusheld, and I know, that's a topic of another discussion. We've covered a lot of ground today. We have these other programs coming up: the one, specifically on COVID, later in July with Nicole Lamanna. The one that you're doing, Nicole, with Dr. Jain, about time-limited therapy. We'll keep getting questions.

But Dr. Richard Furman, Dr. John Allan from Weill Cornell. Thank you so much for being with us, for over three hours, and your devotion to treatments and research. Because look. All of these things you've been talking about, we wouldn't have had if folks in your group and your peers had not helped lead trials to help us give better options. Thank you so much. Rick, thanks, it's always a pleasure and John.

Dr. Allan:
A pleasure.

Dr. Furman:
Thank you, Andrew.

Andrew Schorr:
Thank you so much for being with us.