ASH 2015 Expert Roundtable: An In-Depth Review of Emerging CLL Research

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John Gribben, MD, DSCN, FRCPath, FRCP, FMed
Professor and Consultant Medical Oncologist
Barts and The London School of Medicine and Dentistry, Queen Mary, University of London

Constantine S. Tam, MBBS, MD
Consultant Hematologist, Division of Hematology and Oncology
Peter McCallum Cancer Centre

William Wierda, MD, PhD
Medical Director, Department of Leukemia, Division of Cancer Medicine
The University of Texas MD Anderson Cancer Center

Andrew Schorr:
Hello and welcome to Patient Power. I'm Andrew Schorr. We're on location as we do every year at the American Society Hematology Meeting. This is really sort of ground zero, where news breaks about illnesses we care about. We're talking about CLL. I hang on every word. I've had CLL since 1996 and was fortunate enough to be in a Phase II clinical trial, the FCR trial and it worked. Since 2000, I've had no other treatment. But that isn't the case for everybody. And now we have so many more approved medicines, and others coming; what does it all mean?

Well, we've brought together part of the brain trust in CLL from really around the world, and I want you to meet them. And in the next few minutes, we're gonna extract from them some wonderful perspective for you, the patient or the family member dealing with CLL.

So first I want to introduce you to Dr. John Gribben. Dr. Gribben, you're from the Barts Cancer Institute in London, right?

Dr. Gribben:
That's exactly correct.

Andrew Schorr:
Okay. And how many years have you been devoted to CLL?

Dr. Gribben:
Oh, gosh, I've been working in CLL since oh, the late '80s, early '90s.

Andrew Schorr:
And both in the U.S. and…

Dr. Gribben:
…both in the U.S. and in London, yeah.

Andrew Schorr:
Okay. Now, let's go to Texas, Dr. William Wierda joins us from the MD Anderson Cancer Center in Houston. Bill, what's your title at MD Anderson now?

Dr. Wierda:
I am the section head for CLL in the Department of Leukemia. I'm also the Center Medical Director for Leukemia, so I oversee the inpatient and outpatient leukemia operations at Anderson.

Andrew Schorr:
Okay. And, of course, both these physicians see a lot of patients, do a lot of research. Now let's go over to Australia, Dr. Constantine Tam. Thank you for joining us. And you're in Melbourne, right? What's your title there?

Dr. Tam:
I'm the lead for the CLL and Low Grade Lymphoma Program at the Peter MacCallum Cancer Centre.

Andrew Schorr:
Okay, and we know news that's been coming out of Australia. We're gonna be talking about what had been called ABT-199 venetoclax, now. How's that going to mix in with everything else? And you've been very involved in that, so we want to talk about that, too. Okay. Let's start with you, John. You and I have been talking a long time. And you know me even when I went through treatment many years ago; we used to talk about that. But in the last couple of years, we've had a bunch of new approved treatments, approved in the U.S. and proliferating in some places in Europe, as well. We knew there was promise. How's it panning out?

Dr. Gribben:
I think much better than any of us had hoped or even thought a few years ago. Bill and I were just talking before we started filming about who could have foreseen how far we'd have come in such a short period of time.

You have to remember, for 50 years we had one drug, chlorambucil (Leukeran). Then I think the next big advance was the FC and then the FCR. That combination is great for the small population of patients who are fit enough to have it. We've always had big populations of patients for whom we had no options. The problem's always been that, as you've already said, most people's disease comes back. Each time it comes back, it's been more difficult to treat. It acquires these genetic mutations that don't respond well to chemotherapy.

What all of these novel agents have in common is that they work well in fit and unfit patients. They work well in people who've got the higher risk abnormalities. And what we're seeing at this meeting is they're working even better when we don't wait until patients have truly refracted everything else to use them. So we've been marching them forward, and we're going to see, of course, data at this meeting.

And we've seen the data at this meeting saying how good it is even up front. So huge revolution. What, of course, you've also got is the ability to start to tailor the right treatment to the right patient. It's not about trying to make one treatment fit everybody.

Andrew Schorr:
Okay. And, Bill, clinical practice in MD Anderson, you're seeing people who maybe in years past you wouldn't have had much to offer them whether they were older and less fit, and now you have options.

Dr. Wierda:
We've always tried to have clinical trial available for patients who come to MD Anderson; this is the primary reason why we see patients at Anderson is to do clinical research. And we always have intended to have a trial available for them. Now there [are] even more options, so we have a lot of different options for patients. In the relapse study, for example, now we have almost too many trials available for the number of patients that we're seeing.

We really need to redouble our efforts in terms of educating patients and working on informing them about what their clinical trial options are and to perhaps have discussions that would encourage patients to potentially participate in clinical trials.

Andrew Schorr:
We're gonna talk about that in a minute, particularly in combining drugs in trials, as well.

Dr. Wierda:
Can I just add one thing to what John was saying…

Andrew Schorr:
Sure, please.

Dr. Wierda:
…that I think that for me illustrates how significant the advances have been. For a long time, we talked about clinical trials and looking at progression-free survival as the endpoint. And we never saw improvements in overall survival for a particular trial. And now there's multiple trials within the last three to five years where there's a clear, overall survival advantage just within one clinical trial observation period. So for me, that really illustrates how much we've come in terms of advance of treatment for patients with CLL.

Andrew Schorr:
So basically changing the natural history of the disease.

Dr. Wierda:
Changing the natural history, exactly.

Andrew Schorr:
Okay. Because I remember years ago, we did a program, and a woman was so frustrated. She looked up in a book and it said an always fatal condition; life expectancy may be five, seven years.

She was terrified. And we're changing that for so many people.

Dr. Wierda:
For sure.

Andrew Schorr:
Well, Con, so let's talk about this. We are seeing research going on where maybe there are new classes of medicine that will be added, and you've been involved in that. And so that's very exciting, too, this idea that we'll have other agents operating in different ways—new ways—that can make a big difference. And maybe—maybe, maybe—if we combine them, learn more, maybe will people even get to what we hope could be a cure? I'd love to use that word; that's what we want.

Dr. Tam:
Sure. Certainly we're very lucky to have multiple classes of very active agent, now. So to me, the exciting things are twofold. So first the existing classes are getting redefined. So at this ASH, what we hear about the next generation of BTK inhibitors and the early results.

And how they may be different from already the amazing results achieved by ibrutinib (Imbruvica) in the first-generation BTK inhibitors. And the second thing that I think is exciting, which is not specifically mentioned at this ASH but certainly talked about on the sidelines is the potential to combine multiple classes. You've got new antibodies, you've got your BTK inhibitors, you have your Bcl-2 inhibitors like venetoclax 199. Certainly, we've had some preliminary experience combining ibrutinib and 199 in a different disease, in manta cell lymphoma.

And so far, the results that we've seen are very encouraging. They're not public, but they're very encouraging. And we think in the next year or so we will see a proliferation of similar combinations of highly active therapies across the world in clinical trials. So I think it is a very exciting time to be researching in CLL.

Dr. Wierda:
If I could just pick up?

Andrew Schorr:
Go ahead, please.

Dr. Gribben:
I think what is exciting for all of us is how the science and the clinical work have come together. Now, of course, all of the MD Anderson trials were based on good, solid science that Bill Plunkett and Bill Varshagandi did about looking. But that was about looking about using the drugs we had available. What these drugs have done are targeting pathways that we knew were fundamentally important in the CLL.

So we're really targeting the therapy down to the science of what's happening, and then using that information to go back and using it to come back with real, rational combinations based upon what we know is likely to happen and work well in individual CLL cases. So I think this is a really exciting time for us all to be working on this disease.

Andrew Schorr:
All right, so let's see if we can understand that as patients. So you're finding characteristics of the CLL. Like we used to know—I knew I received rituximab (Rituxan), which was an FCR, and it targeted a protein on the cell and hit it. And it was like a bomb, and it blew it up and it did good for me—not everybody but for a lot of people.

But now you're understanding other things that are fueling the cell, right? And you're trying to cut off these sort of power—things that power it, an escape route story?

Dr. Gribben:
Cut off the fuel supply.

Andrew Schorr:
Yeah, cut off the fuel supply. All right, so is the idea, just like we had with FCR, that if you combine medicines, the cancer in a sense can't escape. Bill, do you want to talk about that?

Dr. Wierda:
Sure. That's the rationale behind combining these agents and targeting different mechanisms at the same time that our survival signals, for example, for the cell so if you block BTK and you're blocking Bcl-2, for example, then you're hitting the cells. These drugs don't have overlapping toxicities, necessarily so you can—patients will relatively well tolerate them together. The CLL cells have less of an opportunity to develop resistance and to survive that double hit of toxicity to them.

Andrew Schorr:
Let me just follow up on one thing about that resistance. So we've seen in some other conditions a concern where you take a single medicine, and it works great, but it doesn't keep working after a while. So that's resistance, where the cancer kind of figures a way out. So is the idea if you combine medicines all at once, that cancer can't develop that resistance?

Dr. Wierda:
Right. Or there [are] fewer cells that are potentially able to develop that resistance.

Andrew Schorr:
Okay. So you've been involved in research. They have, too, but what we had called ABT-199, venetoclax, you and Dr. Seymour in particular. So there's been a lot of buzz about that. So how would that work in combination with ibrutinib or some of these other medicines that we have?

So your question was about how the two drugs may work. I think from Varsha's lab and also from Varshagani's lab and also from Metho David's lab, we've seen some results where they've combined different drugs and looked at the effects on cells in the test tube. And certainly one of the most promising signals to come up is the combination of a BCL receptor antagonist like ibrutinib and a Bcl-2 antagonist like venetoclax.

That in itself is very promising because the laboratories have told us that when you mix different drugs, that this is probably one of the most active combinations. Now, from my practical sense, these are two drugs which are both taken by mouth as tablets, so they're convenient to give.

And as Dr. Wierda mentioned, they don't really have overlap in toxicity so we can put them in a patient, and we won't get horrible overlapping side effects, because one drug causes nausea. The other drug caused nausea, so you get very bad nausea. It's not like that. The toxicities are different. Lastly, when it comes back to your point about resistance, we don't understand why resistance happens. But we think that either the cells evolve under the pressure of treatment, or maybe amongst the many, many cells in our body, it's based on the one or two cells that carry the resistant gene already. And if—suppress everything and allow those cells to grow up.

Andrew Schorr:
Stronger cells.

Dr. Tam:
Stronger cells. But if you think about it mathematically, it is highly unlikely for a cell in a given patient to be resistant to a potent drug like ibrutinib maybe one in 10 billion or something like that.

And if you find—put a second drug in, that one in however many billion cell also has to be resistant to the second drug. So the probability goes even lower and gets to a point where they're probably lower than the number of cells in a patient's body which are cancerous. And so it is possible that with combinations of two or three highly potent drugs, they will get to a stage where there will be more resistance. But only time will tell.

Andrew Schorr:
Okay, well that's what we'll learn about in trials. So let's talk about where we're headed. You're gonna do different combinations, and we'll talk about people being in trials and the benefit to that. But when you develop cancer, your immune systems let you down. There's been a lot of buzz about the immuno-oncology in solid tumors, etc. Can your immune system be helped, just like a transplant helps it, and kind of a—if you can tolerate that—with these checkpoint inhibitors that we've talked about in other illnesses to help fight the cancer. Bill, do you want to comment on that?

Dr. Wierda:
Sure, and probably John is in a better position to comment on that, because he's generated a lot of the laboratory studies that have been the basis for what we're doing now in the clinic. I, several years ago, was looking at one of these checkpoint inhibitors referred to as CTLA-4, and we found that there were increased levels of CTLA-4 expressed in T cells of patients with CLL. CTLA-4 is a way that the immune system will down-modulate the activation in T cells. And so the T cells in patients with CLL have higher levels. And in the lab we showed that if you block CTLA-4, you could reactivate T cells against patients' own leukemia cells.

And so for a long time, I have intended to do clinical trials in these antibodies. The original antibody that was studied clinically was a drug that targeted CTLA-4 called ipilimumab (Yervoy). It was very difficult for us to get access to that for patients with CLL.

Nevertheless, it went forward, and there's clinical activity in solid tumors. We still haven't been able to test it in patients with CLL. The toxicity is a little bit high. It has a high side effect profile. And there's another checkpoint molecule that John can discuss I think better than I can in terms of the laboratory investigations but it's referred to as PD-1. It's overexpressed—or there's high levels of expression of PD-1 also in T cells of patients with CLL. And there's an antibody that targets PD-1 that appears to be a little bit better tolerated than the CTLA-4 antibody. So we've recently opened—and it's called nivolumab (Opdivo).

And it's a Bristol Myers Squibb drug that they've gained approval in solid tumors. So we have a trial that just recently opened with nivolumab plus ibrutinib for patients with CLL. I'm optimistic that we'll not only see activity in terms of treating the CLL but also some evidence of immune reconstitution; fixing the defects that patients have in their immune system that predisposes them to develop infections and, perhaps, second cancers; skin cancers, etc.

Andrew Schorr:
John, let me see if I understand this, and you can add your perspective. So our immune system let us down, if you will, and we started—the CLL cells proliferated. So this is the idea that we can help the immune system do the job that it didn't do that time.

Dr. Gribben:
Sure, and it's a little more complicated than that. There are some cases where your immune system fails, and you develop cancer. It looks very much in CLL as if something else happens; you develop CLL. And CLL is very effective at switching off the immune system to be recognized. So it's not like some lymphomas that come from viruses in people whose immune system is suppressed. We've got very clear data that it's the CLL itself, which is very immuno-suppressive.

Andrew Schorr:
It's like stealth. It has like a shield.

Dr. Gribben:
Confounded by the fact that treatments that we have like fludarabine (Fludara) really, as well as killing off the CLL cell, killed off a lot of the immune system. So we've spent a lot of time trying to understand what was wrong with the immune system in CLL. We could see clearly by any measurement that you did that T cells and K cells, B cells in individuals with CLL didn't work very well, as everyone with CLL knows in terms of the risk of increased infections.

We did a lot of work trying to understand at the molecular level why that happened and found out that one of the most important molecules that did this is the PDL-1 molecule that is the one on the CLL cell that sticks onto the PD-1 on the T cell that Bill's got the clinical trials running on, now. And so we had very clear evidence in CLL this was an important molecule. Actually, long before it was being developed in the solid tumors, the issue was, of course, that the companies were much more interested in developing it for the bigger markets.

But I think we had very, very strong evidence to suggest that this was gonna be a really effective target here in this disease. And, of course, another huge advantage is the toxicity profile looks pretty low. So again, another whole arm you could add into the other types of treatments we've been talking about.

Dr. Wierda:
Just to add to what John's saying, he mentioned PDL-1. We also have a clinical trial with another monoclonal antibody that's directed against PDL-1, which is again the molecule…

Andrew Schorr:
...so PD-1, PDL-1…

Dr. Wierda:
Right.

Andrew Schorr:
Okay.

Dr. Wierda:
But the PDL-1 is on the CLL cells and that's how they suppress the T cells.

Andrew Schorr:
But all the ideas to help the immune system do its job and help the CLL cell be recognized.

Dr. Gribben:
What you'd really hope is that, as Con was mentioning earlier, if you've got a cell that's in there becoming resistant to BTK inhibition, what you're really hoping at the same time is we can use someone's own immune system as it recovers to go in and attack those cells. So you're looking to attack those cells from every direction.

And really what we want to get to—don't get me wrong; it's a great advance. We've got agents like ibrutinib and ABT-199 that you could go onto and take for the rest of your life. But I think what all of us are looking for is you get rid of the last cell, and you stop the last treatment and you're off it, and we've really cured the disease. And at the speed with which things have been changing in this disease, I'm really optimistic that we will get there.

Andrew Schorr:
Really? So the C word could be cure?

Dr. Wierda:
Soon.

Dr. Gribben:
Soon, yeah.

Andrew Schorr:
Really?

Dr. Tam:
Yes, absolutely.

Andrew Schorr:
So you hear that, folks? We're talking about cure with this different science coming together with more power; power to outsmart the CLL cell, which has been…

Dr. Gribben:
Pretty smart.

Andrew Schorr:
…pretty smart. Widely. Okay. So that means, then, can we hope that even if we're taking powerful medicines now and they're working pretty well, they're not without side effects; there's no free lunch with powerful medicines. But many people do pretty well, or there's another medicine they can switch to, now, that may not have the same side effect profile. But we all hope we can be without medicine and go on with our life.

So are you saying—when you see patients, can you say I'm working in the lab and I'm also seeing patients, I can see that day coming? You can?

Dr. Tam:
Yes, I do. I think from our younger patients, what I tell them is you have a disease that we conventionally think it's incurable. We've got very good treatment for it, but we conventionally think it's incurable. But the rate at which things are moving, we may well be seeing the cure in your lifetime.

Andrew Schorr:
Yeah, you'd be out of business, Con. You'd have to go and do something else.

Dr. Tam:
I can always go sell galati or something else.

Andrew Schorr:
Okay. So let's talk about one other area that there's been buzz about. And that is these CAR T cells, okay? Let me ask you first, Bill. So the idea was could you make a medicine that, again, working on the immune system, had been expensive to make? There's been some talk could there be sort of an off-the-shelf approach where you add something from the patient, but you have kind of a foundation, and it's cheaper.

Where are we with that? Is that still out there?

Dr. Wierda:
It's still out there for a couple of reasons. So for sure there's activity in using the CAR T cells directed against CD-19 to treat patients with CLL. There [have] been reports. The U Penn group has reported excellent outcomes and long-term remissions for patients who've received the—patients with CLL who have received CAR T. There's toxicity associated with it, and it's not insignificant toxicity. So nearly a quarter of the patients end up needing intensive care unit level care during their initial portion of treatment.

For patients who are on ibrutinib or have all these oral options, and they're working and doing relatively well, that's a hard pill to swallow. So it's gonna be initially a treatment that we talk about with patients with very high-risk disease that we're very worried about or who may be failing and becoming resistant to these newer, more effective agents.

There [have] been a lot of resources that have been directed at developing the CAR Ts. There are pharmaceutical companies that are involved now. It's very expensive. It's a whole, new treatment. There isn't really anything that's like it other than transplant. And so it requires a lot of reagents that are new and different. It's a personalized therapy. There are production facilities that they've had to develop just to do the clinical trials.

And so that's been a slow process, because it's completely new. It's a completely new strategy. And a lot of the infrastructure that's been built has been built just to initiate the clinical trials. And the initial clinical trials have been written to treat ALL, which is a very aggressive type of leukemia. ALL and diffuse large B-cell lymphoma. So these trials are now opening.

We'll be treating those patients with CAR Ts initially with DLBCL or ALL. I think we'll learn a lot during that experience. It'll become safer; we'll know how to better do it. And then the time will come for CLL, and we'll have that. It's gonna be a year or two off, I think, before there's a significant number of trials that open for patients.

Andrew Schorr:
Okay. So, John, I know there are just some headlines from this conference, and you're a chair of one of the sessions. I know that there's data about ibrutinib having effectiveness for older patients earlier. And you talked earlier about moving drugs earlier. So is that where we're headed, now, with these new agents that have been approved for second line not just for older patients, and not just with certain subtypes of CLL but for a broader group we can use these pills earlier?

Dr. Gribben:
Sure. At this meeting, we've got the results of the Resonate II trial, front-line treatment; ibrutinib versus chlorambucil. It's in the *New England Journal* this weekend—so right out there, outstandingly good results.

I think everybody knew that ibrutinib was probably going to be better than chlorambucil on the basis of how effective it was for very end stage patients. But I think the results are just outstanding. And it's very, very clear, now, that you are seeing better results the earlier you treat a patient. A big—slight but not let's say a big concern—a concern still remains if you use your best drug first, what does that leave you for later? I think in many respects that's also becoming a little bit of an old-fashioned idea.

Bill mentioned earlier we've seen trial after trial showing survival advantage for what we're doing by using our optimal therapy first. And probably I think this will become a treatment widely adopted I think even without licensing approval. At the moment, a lot of clinicians are using it.

We're certainly using it for patients who've got high-risk features at our presentation. There's been a big trial looked at watch and wait versus ibrutinib, which we haven't seen the results of yet. But moving it forward seems to be a large component of what we're doing. What, of course, we also hope will happen is that it won't induce the kind of high-risk genetic features that the chemotherapy did. One caveat for all of these trials is that each one of those trials showing these new agents has been so much more success than the other agent. We've had a positive readout of the trial quite quickly; much more quickly than we've ever been used to with trials.

That's great for patients because it got approval for these drugs very, very rapidly. But it does mean that when we're talking about long-term follow-up here, we're talking about one and two and three years on these trials. We really do need longer follow-up of these sorts of agents to really understand what impact alone they're going to have overall.

Andrew Schorr:
Okay. You mentioned about combinations. So the ideas can the drugs—we're moving some drugs up earlier as single agents, like ibrutinib maybe will be used for a lot more people right off the bat. Okay, so the ideas, though, he's saying what may happen two, three years. Are we shooting ourselves in the foot? We're getting great benefit now, but are we creating some other situations down the road? That would be the concern, right?

Dr. Tam:
It would be some concern, because we do know in the relapse setting that the rate of, let's say ibrutinib, related with mutations do rise after two years and beyond. On the flip side, with the front-line setting the response is simply more durable. There seems to be less cases of resistance being developed, albeit with shorter follow-up. So we can see the situation where when you treat the leukemia when it's not as genetically complex, that maybe you can get more durable control.

I guess the concern in a lot of our minds is actually the cumulative toxicity and cost of long-term treatment for these patients. Now we've moved to a point where probably the best treatments available are front line now, and patients are living for a very long time in good health. Nevertheless, these drugs are not without side effects, as you pointed out. These drugs are very expensive. And what I meant was really now is how do we stop people from being on one of these drugs indefinitely, for the rest of their life, and how do we take the next step forward?

Which is why, as you mentioned before—and as Bill mentioned before and as John mentioned, cure I think is what we're aiming for. A limited duration of therapy; get rid of the last cell, stop the drugs.

Andrew Schorr:
Okay, I just want to summarize for a minute, and then I just want to ask about clinical trials. So what you're saying is there's a broader brush of patients, the wide group of patients now, you have medicines for them. Many of these medicines can be used earlier.

We still have monoclonal antibodies that have a place, right? So some people will still get some infused therapy, and there will be some people who still get some chemo. FCR still has a place for some people, I know, and certainly it's less costly than some of the other medicines, as well. But you're working on combinations that hopefully can get us to a point where you then can go off medicine; maybe someday your immune system can take over. Did I get it right?

Group:
Absolutely.

Andrew Schorr:
Okay. So that relates to clinical trials. You're all involved in research. It's really a low percentage of patients who are in trials. So what do you say to people about considering being in trials, particularly as you figure out these new combinations that are trying that long-term effect? What do you say to your patients, John?

Dr. Gribben:
Every study has shown that the outcome of patients on clinical trials is better than it would be if patients were not able to have those trials. There are very powerful safeties built into trials.

So the idea that someone's just a Guinea pig and being exposed to something isn't really beneficial; it's been proven wrong. Some of the people who, of course, went on the early ibrutinib and idelalisib (Zydelig) trials and the ABT-199 trials, I've got no doubt would not be alive had they not entered into those clinical trials and those trials being so successful. It is through the clinical trials mechanism that we are able to really move these fields forward, work out what the toxicity profiles are. And it's without clinical trials we aren't going to get to this cure the three of us are certain we're going to get to. That's the only way in which we're going to be able to get there.

Andrew Schorr:
You're all nodding your heads.

Dr. Wierda:
And I think one of the things that patients worry about, or the next word that comes to mind when they hear clinical trials is placebo; and am I gonna get a placebo. That's the main question I get, the first question I get when I start talk about clinical trials with patients.

And although there have been clinical trials done relatively recently—there was an idelalisib trial that included a placebo—I think right now there are so many agents, the standard of care requires some treatment, whether it's one of these small molecule inhibitors and/or the addition of a CD-20 antibody that it's really unethical right now to develop any clinical trials that have a placebo arm in them for patients with CLL.

Dr. Gribben:
Actually I can go further and say that the control arm is now very often a really good way of getting an incredibly effective treatment without cost. Because even the control arms are becoming so good. It's one of the hurdles that we have that we've maybe raised the bar so high for ourselves that to show benefit over some of the outstanding results we're seeing at this meeting is going to be quite difficult.

Dr. Wierda:
So if you hear clinical trial and CLL, you're gonna get good treatment, whether or not you get randomized. You may get the addition of a placebo, but the primary treatment is not gonna be placebo; it's gonna be some effective treatment.

Dr. Gribben:
And lastly, almost all of the trials are built into it. That if it looks as if one arm is secure with the other, there is the opportunity to switch.

Andrew Schorr:
Okay. You endorse all that? It's the same in Australia?

Dr. Tam:
Absolutely. When I talk to my patient about clinical trial, the first thing I say is I'm not happy with the way your disease is being managed. We've made great progress, but we're not there yet, and we can do better. And what clinical trial is about is how can we do better. We have got very good standard already, but how can we do better? And the worst you can do when you go into clinical trial is to get the best conventional therapy available.

Andrew Schorr:
Okay. I'm just going to give you a chance to make a final comment. What do you want to say? I'll start with you, Con. What do you want to say to patients who are watching? Many have been living, thank God, with CLL for many years now, but there are newly diagnosed people, people with what you call higher risk disease. From where you sit, what do you want to say to them to give them hope?

Dr. Tam:
I want to say that I think I'll speak for the three of us when I say that the progress over the past five years have exceeded all our expectations. I don't think any of us could have expected to be where we are right now. And we will build on that progress to make treatment better. So continue to be hopeful, continue to keep up with the information, and continue to work to support all of us in getting to that goal.

Dr. Wierda:
I think the comment that I would make is, so I've been involved in CLL research for almost 20 years, now. In the past, we didn't have, in the research groups that we work with in the CLL Research Consortium, we didn't have substantive discussions about cure. Now, that's a topic. And that's an intent with regard to all of our clinical trials. So cure is a much more—t's a word that's used. In the past, people sort of used to cringe talking about cure, etc.; is that really possible?

I think now with all these agents, that is possible, and I think we see that that's possible. And I think many of us who do clinical trials and clinical research are working towards that end.

I don't remember. Final comment from you, John?

Dr. Gribben:
Sure. I think this is a really exciting time for CLL, as we've all been discussing. But for those of you out there who've got the disease that needs treated, find a clinical trial if at all possible. Get yourself onto the best available treatment that's available to you that you can have. There's bound to be a clinical trial. Asking a really important question that's suitable for your particular circumstances; seek it out. Use the resources that are available to find that trial and get the best treatment you can.

Andrew Schorr:
I would just say from the patient's perspective, and I was in a Phase II clinical trial, and I went from Seattle to Houston to your medical center to do that, and there was tremendous collaboration with my community doctor who I liked a lot, but he was not a CLL specialist.

If things are changing, and they are at a rapid change, and these gentlemen are right where it's happening. They're involved in this change and they're talking to one another. You want to at least have a consultation with someone like that and say what are my options now, including clinical trials, including new approved therapies. Can drugs be combined for greater power for you? And hopefully working together as a community with these researchers, we can get to a cure. And I hope we can.

I want to thank you on behalf of the CLL community for your devotion worldwide in what you do. I've known a lot of you for many years. I hope I can know you for many more. And then we can have a big party and celebrate a cure. Wouldn't that be great?

Dr. Wierda:
Sure.

Andrew Schorr:
Okay. Thank you for being with us from ASH in Orlando, Florida. We'll continue to bring you the news worldwide. And we hope that this brings you hope, knowing that you can do better with CLL. And if it's your loved one, hopefully we can all be celebrating together for a long time to come. In Orlando, Florida, I'm Andrew Schorr from Patient Power. Remember, knowledge can be the best medicine of all.