This transcript was lightly edited for readability.

Introductory Remarks

Moderator, RTI International

Thank you, **[REDACTED]**. I appreciate it. And thanks to all of you for coming today. I'm **[MODERATOR]**, and I'm from RTI International. I also want to introduce my colleague **[SECONDARY MODERATOR]**, who you may hear from at a few points in the discussion.

The Centers for Medicare & Medicaid Services, CMS, is convening this patient-focused, roundtable event, and others as part of the Medicare Drug Price Negotiation Program. The purpose of today's event is to hear from you all, a group that may include patients, caregivers, and patient advocates about your experiences with the conditions and diseases treated by Calquence, with Calquence itself, and with other medications for the same conditions.

The information shared during the events will help CMS understand patients' experiences with the conditions and diseases treated by the selected drugs, patients' experiences with the selected drugs themselves, and patients' experiences with other drugs that are used to treat the same conditions.

CMS may use this information in negotiating Medicare pricing with the manufacturers of selected drugs. Your experience and perspectives are very important to us, and we genuinely appreciate your time today.

Let's watch a brief welcome video from CMS leadership so that you can hear from them about how much they value your time and input firsthand.

CMS Remarks

00:01:28

Steph Carlton, Deputy Administrator and Chief of Staff, Centers for Medicare & Medicaid Services

Greetings, everyone. I'm Steph Carlton, the Deputy Administrator and Chief of Staff at the Centers for Medicare & Medicaid Services, or CMS. CMS administers Medicare, our country's federal insurance program, for more than 65 million older Americans and people with disabilities.

I deeply appreciate each one of you for taking the time to join us today. Lowering the cost of prescription drugs for Americans is a top priority of President Trump and his administration. As the second cycle of negotiations begins under the Trump administration, CMS is committed to engaging with stakeholders for ideas to improve the Negotiation Program.

In January 2025, CMS announced the 15 Medicare Part D drugs selected for the second cycle of price negotiations. Medicare's ability to negotiate directly with drug companies will improve access to some of the costliest drugs while fostering market competition and continuing innovation.

Our priority in negotiating with participating drug companies is to come to an agreement on a fair price for Medicare. Promoting transparency and engagement continues to be at the core of how we are implementing the Medicare Drug Price Negotiation Program. And that is why the process for negotiation engages you, the public.

This event is part of our effort to hear directly from a range of stakeholders and receive input that's relevant to the drugs selected for the second cycle of negotiations. Thank you again for joining us. Your input matters. And next, stay tuned to hear from the event moderator to give you more details on what to expect during this event.

00:03:25

Moderator, RTI International

Great, and I also want to make you aware that staff from CMS will be sitting in on this event so that they can hear your experiences and opinions directly from you. In fact, let me go ahead and hand it over to them for a moment, so that they can say hello.

00:03:41

CMS Staff

Thank you, **[MODERATOR]**. We want to thank everyone for coming to this roundtable event. We will be here listening. But we want to stay off camera so that we can focus on you guys' discussion. But we will be here throughout the whole event, listening and taking notes just for your benefit. Thank you.

Housekeeping

00:04:00

Moderator, RTI International

Great. Thank you. **[CMS STAFF]**. Okay, before we begin, I just want to review some quick housekeeping items and ground rules so that everyone knows what to expect today. First off, participation. We really hope that you'll all contribute your perspectives throughout the session. However, if questions arise that you don't want to answer, that's okay.

Thank you very much for minimizing background noise by silencing your cell phone and other devices, if you haven't already. Just another reminder to please mute yourself when you're not speaking.

In terms of privacy, this discussion is not open to the press or the public. We will use first names only during the discussion to protect your privacy. Please do not share any unnecessary personally identifying information or personal health information during the discussion. We are video and audio recording today. But these recordings will not be shared publicly.

Following the event, CMS will prepare transcripts that have participant names and identifying information removed, and these will be available to the public.

In terms of video, thank you very much in advance for keeping your video on throughout the discussion. I appreciate that. The timing is such that the session will last for about an hour and 30 minutes. I do have a discussion guide in front of me, and that's just to help me stay on track.

We have a lot of different topics to cover today, so you may see occasionally that I'm redirecting our conversation or cutting a conversation short at times. And that's really just to make sure that we can cover everything, not that we wouldn't like to hear more about that topic.

In terms of technical assistance, if you would get disconnected for any reason, please just attempt to rejoin. If you can't connect, please reach out to IRADAPStechsupport@telligen.com, the address that's on the slide.

If you do need to step away briefly during our discussion, that's no problem at all. Just turn off your camera and microphone and rejoin when you're able to. You don't need to tell me that you'll be away from your computer. Please just return to the discussion when you're able to.

In terms of speaking, please try to speak one at a time. I may occasionally interrupt you when two or more people are talking, just to make sure that everybody gets a chance to talk, and that we can hear everybody's comments, and that they're accurately recorded.

Please feel free to use the raise hand feature in Zoom and take a moment to find that feature if you haven't already. That'll help us know when someone would like to add to the discussion. You can also always enter your comments in chat.

Last of all, your opinions and experiences will differ, and we want to know what each of you honestly thinks about the topics that we're discussing.

Does anyone have any questions about these housekeeping items before we get started?

Okay, hearing none. Let's jump right in. I would like to begin our discussion today by asking each of you to introduce yourself. I'm hoping that you'll each take about 30 seconds to tell us your first name, the condition or conditions that Calquence treats that you have experience with, and whether you'll be sharing personal experiences or those of a loved one, or whether you're sharing patient experiences from the perspective of a patient advocate.

I'll go ahead and call on each of you in the order that you appear on my screen again. We're going to keep these to about 30 seconds, real brief.

[Participant 1]?

Discussion

00:07:39

Participant 1 (registered as a representative of a patient advocacy organization)

Hi! I'm **[Participant 1]**. I'm filling in for **[REDACTED]**, a patient who couldn't be here today, and who you originally selected for the roundtable. I also work with CLL [chronic lymphocytic leukemia] Society's Policy Institute and have heard from both CLL patients and the CLL experts on CLL Society's Medical Advisory Panel.

I have also spent a good deal of my professional life advocating for patients with rare and especially ultra rare conditions. So, that's three hats I'll be wearing today.

00:08:09

Moderator, RTI International

Thank you, **[Participant 1]**. What about you, **[Participant 2]**?

00:08:13

Participant 2 (registered as a patient)

My name is **[Participant 2]**. I am a patient with small lymphocytic lymphoma, the SLL part of CLL/SLL and I'll be sharing my experiences.

00:08:25

Moderator, RTI International

Great. Thank you, **[Participant 2]**. What about you, **[Participant 3]**?

00:08:30

Participant 3 (registered as a representative of a patient advocacy organization)

Sure, so I am a patient with chronic lymphocytic leukemia, CLL. I was diagnosed just about three years ago, now. Still awaiting treatment, but also, since my diagnosis I've begun working with CLL Society, so I'll be sharing primarily my personal experiences, and where I am in my CLL journey, but also a little bit of information pertaining to my role with the CLL Society.

00:09:01

Moderator, RTI International

Thanks, **[Participant 3]**. **[Participant 4]**?

00:09:07

Participant 4 (registered as a patient and representative of a patient advocacy organization)

I'll be wearing a few hats, too. Primarily I'm a CLL patient since 2005, and I like to call myself a clinical trial junkie, been in multiple clinical trials and benefited from the class of drugs that acalabrutinib is in, was in a phase one trial of **[REDACTED]** that later became Ibrutinib.

My role as a **[REDACTED]** led me to make sure that other patients had the opportunity to get their best possible care, led to me **[REDACTED]** and now I serve as the **[REDACTED]** of the nonprofit CLL Society, and will be bringing that kind of experience that I have as a physician and patient advocate, as well as a patient myself.

00:09:55

Moderator, RTI International

Great. Thank you. **[Participant 5]**?

00:10:02

Participant 5 (registered as a patient)

Oh, here!

00:10:03

Participant 6 (registered as a patient)

Thank you for this opportunity to speak. My name is **[Participant 6]**. I've been dealing with CLL for 20 years, and I'll be providing my own experiences.

00:10:18
Moderator, RTI International

Thank you, **[Participant 6]**. And what about you, **[Participant 5]**?

00:10:22
Participant 5 (registered as a patient)

Yes, my name is **[Participant 5]**, and I was diagnosed with chronic lymphocytic leukemia in 2000. Over that time, I've had seven different protocol treatments, including three clinical trials and also one registration trial for Ibrutinib **[REDACTED]**.

00:10:51
Moderator, RTI International

Thank you, **[Participant 5]**. And **[Participant 7]**?

00:10:54
Participant 7 (registered as a representative of a patient advocacy organization)

Yes, hi, I am **[Participant 7]**. I am with Cancer Support Community, so we are a nonprofit that provides psychosocial support for people impacted by cancer. And one of the things that we do is we have a cancer experience registry where we capture the patient experience for patients, caregivers, and survivors. And so what I will be doing is providing those patient insights for individuals diagnosed with chronic lymphocytic leukemia, small lymphocytic lymphoma, and mantle cell lymphoma based off of the insights from our longitudinal survey.

00:11:30
Moderator, RTI International

Great. Thank you, **[Participant 7]**, and you answered the question I was about to ask, which was whether anybody would be able to represent the perspective of mantle cell lymphoma [MCL]. So, I'm glad to know that you'll be able to share experiences related to that as well.

Okay, great. Now that you all have introduced yourselves briefly, I would like you to use the chat feature to say, to share some more information that will be helpful for me to know before we go forward. Have you or a loved one taken Calquence currently, or in the past? Please enter a yes or no in the chat.

Okay, all right. Thank you very much. That's helpful to know. So, thank you again for being here today, and thank you for introducing yourselves and telling us the experience that you'll be drawing from today.

Let's start by talking about your or in general patients' experiences with the conditions treated by Calquence. We know that there will be a lot to talk about with this question, so please feel free to raise your hand and share briefly, and or again enter comments in the chat as needed. I do want to give you a heads up about a few things. Given that Calquence treats multiple conditions.

I want to let you know that for each topic I'll first be asking about chronic lymphocytic leukemia and small lymphocytic lymphoma, and then I'll be repeating my question for mantle cell lymphoma so that we capture both perspectives for both sets of conditions. Also given that the condition names are kind of a mouthful. Please note that I may sometimes just be referring to the conditions by their acronyms, CLL, SLL, and MCL.

So okay, right, let's go ahead with the next question. In general, how does CLL or SLL affect patients' day-to-day lives, and if you want to raise your hand, if you want to speak or just jump in. Let's start with you, **[Participant 3]**.

00:13:52

Participant 3 (registered as a representative of a patient advocacy organization)

Yeah, I'll jump in. And just to start, I'm relatively new, I guess, in this world. I know many of the people on the call were diagnosed long before I was [b]ut I think what I would stress is that it really, this is a disease that affects everybody in different ways. I mean we like to say at CLL Society, if you know one person with CLL, then, you know one person with CLL. It's not, you can't extrapolate that experience to the CLL community. And some people right from the beginning, from their diagnosis, need treatment. Other people go for many, many years, or even the rest of their life without needing treatment.

So, just to bring that to my own personal experience, I'm somewhere in the middle three years from diagnosis. I'm looking at treatment probably in the next two years. I have a form of CLL, it's unmutated, which means it's a little bit more aggressive, typically faster growing. And that's been my experience. But I know other people who were diagnosed the same time as me, who have had absolutely no progression in their disease at all. So, just sort of starting out just to make that point that really everybody along their journey experiences so many things that are different from everybody else on the same journey.

00:15:26

Moderator, RTI International

Thank you, **[Participant 3]**. What about you, **[Participant 5]**?

00:15:30

Participant 5 (registered as a patient)

Well, because I have had CLL for 25 years, I've experienced a lot in that journey, and it highlights the fact that CLL is a chronic disease. But right now, typically you can say there's no cure for it. And most people that have treatment at some point in time, that treatment becomes ineffective, and they have to move to a second or third or fourth treatment. And that's why it's important to have multiple options available for patients when they do relapse so that hopefully, they can get the CLL under control again. And that's why I think it's really important that even though we have a BTK [Bruton's tyrosine kinase] inhibitor originally approved for CLL, that we need multiple options just like **[Participant 3]** said, no two patients react the same to drugs. No two patients have the same adverse events. And that's why multiple options for patients is so important.

00:16:33

Moderator, RTI International

Thank you, **[Participant 5]**. I'm gonna turn to you next, **[Participant 6]**.

00:16:39

Participant 6 (registered as a patient)

Thank you. I was diagnosed with CLL in 2005, basically, 20 years ago. I had no symptoms at the time, like a lot of people. My CLL was discovered during my annual physical. I started needing treatment in 2010, even though my numbers and physical symptoms were maybe halfway to the

guidelines of when to start treatment and stop watching weight. But I had a particular physical problem. I had a lymph gland in my throat that was so swollen I couldn't swallow bulky foods.

So again, even though my numbers weren't at the point where traditionally you'd start treatment, I had to start treatment. At that time there weren't a whole lot of options, so I had to go on chemo.

I have three bad blood markers and was warned that even though the chemo got me into remission, what they call complete remission, the cancer would come back. And that's what happened about two and a half years later. In 2013 the thing in my throat grew again. And again, my numbers weren't that bad, but it was time to do another treatment. This time the recommended treatment was a form of chemotherapy called bendamustine plus rituximab. Unfortunately, they were useless to help me because of my bad markers.

One of the bigger impact that this is having on me, or that CLL has had on me, is immune system problems. The CLL damages the immune system itself, and then the treatments make a bad situation worse. Since I travel to fairly exotic locations, and the vulnerabilities were a huge struggle, I really needed to minimize the side effects, etc. and control my immune system problems.

00:18:44

Moderator, RTI International

Thank you, **[Participant 6]**. **[Participant 4]**?

00:18:51

Participant 4 (registered as a patient and representative of a patient advocacy organization)

Like **[Participant 6]**, I was diagnosed almost 20 years ago, when the options weren't very good. Like **[Participant 6]**, my diagnosis came as a surprise when I had blood work for something else, and found out that I had chronic lymphocytic leukemia. And when you first look at this, even as a physician, the words that come up are incurable and chronic.

I can't emphasize enough how variable it is from person to person. I had terrible markers, and my disease followed what my biomarkers would say, and was in a world of pain within the first year, with multiple hospitalizations for autoimmune complications of the CLL. I had what's called ITP, immune thrombocytopenic purpura, where I attack my own platelets. This is not an uncommon complication in CLL. There's others like autoimmune hemolytic anemia, which is a little more common. Multiple hospitalizations, emergency surgeries, internal bleeding... I was... and with great clarity that the therapies that were available, chemoimmunotherapies, wouldn't work for me because I had markers that said they just wouldn't already suppress an already corrupted immune system.

I went for an unusual course. I went, some of the treatment for my ITP got me into a partial remission. I went for a bone marrow transplant. It didn't work. I tried a little of this, a little of that. Some really off-the-wall kinds of therapies that were immunosuppressive but managed to jump on a phase one trial of **[REDACTED]**, which later became Ibrutinib. I responded wonderfully to that for seven years.

And then, when I relapsed, I went on to a trial of **[REDACTED]**, which later became liso-cel, which is a CAR-T [chimeric antigen receptor T-cell] therapy. And right now, I'm on a third clinical trial of epcoritamab, which is approved in follicular lymphoma, diffuse large B-Cell lymphoma but not in CLL. And actually, I'm **[REDACTED]** on this trial, and I'm doing fabulously well on it, thank God. So, I'm a big believer in the science breaking through. But the whole point I'm trying to make with my

story, and I think with **[Participant 5]**'s story and **[Participant 6]**'s story is that, with CLL, you're going to have a chronic illness. Everybody's going to react different. And you're going to need a lot of kicks at the can down the road because there are no therapies at this point that are curative. So, each one of us has to have different options that are available, and sometimes that option is a radically different mechanism of action, and sometimes it's the same medicine, but it's better tolerated, or it has a different half-life, or it has a different absorption profile, and even that little difference can make a difference.

The other thing that I see that's positive that's happening in CLL is that we're starting to look at more limited-duration therapies where there may be some times off of therapy for patients. So, these are things that I see positive. But as a patient and as a patient advocate, we can't have enough options available to us, because in all likelihood, especially those of us who are diagnosed at a younger age are going to need lots of therapies, because one therapy is not likely to cure us. God willing, that'll change, but it hasn't changed yet.

00:22:22

Moderator, RTI International

Thank you, **[Participant 4]**. I appreciate it. And I was able to hear everything you said, but going forward, if you could speak up just a little bit more, if possible. So, make sure that everybody is able to hear you well. Let me go on to **[Participant 2]**.

00:22:39

Participant 2 (registered as a patient)

I was diagnosed in 2015 with small lymphocytic lymphoma, which is the lymph node version of this disease. Because of that, my blood work in labs had always been normal. So, it was surprising that I was diagnosed with this. It's the less common version of this disease. I do have intermediate to high-risk markers. So, it was 22 months after diagnosis that I required treatment.

I was fortunate. I was right on that cutting edge of these new drugs being approved, and I was able to get into a clinical trial for **[REDACTED]**, which became Calquence, and I responded really well to the Calquence. I was on the trial for about five years. I had lymph nodes the size of grapefruit, orange, and lemon, and extreme fatigue, and those were the initiating factors for treatment. So, the lymph nodes reduced really rapidly with Calquence, and it was well tolerated in terms of side effects, some bruising, some headaches. All of this was easily managed, and I'm in partial remission now for about four years. They call it partial remission, because with lymph nodes that get that large, they don't shrink back to normal size. So, the drug was completely effective. I completely responded to it, but we call it a partial remission. And I just want to say, in adding to what others have said about needing multiple treatments, I was diagnosed at age **[REDACTED]**, which is relatively young. So, I know in my life, since I have intermediate to high-risk markers, I will probably need multiple treatments in my lifetime. So, it's really important to have options.

00:24:40

Moderator, RTI International

Thank you, **[Participant 2]**. I appreciate you sharing all of that. And **[Participant 7]**. I'm gonna turn to you now. And before you get started, I wanted to let you know that I did see your clarification in the chat. Thank you.

00:24:50

Participant 7 (registered as a representative of a patient advocacy organization)

Yes, absolutely. So, CSC, we have a cancer experience registry, as I mentioned, and our 2020 report on chronic lymphocytic leukemia includes data from 191 CLL patients and survivors in the U.S. at various stages of diagnosis and recurrence. So, I'm going to focus on these patients.

So, our report found that 34% of patients reported that CLL affects their ability to work, and 42% reported that CLL affects their day-to-day finances. Our analysis also found that CLL patients reported quality of life significantly worse than the average American. A couple of examples, almost a quarter reported worse fatigue and anxiety; 15% reported worse physical function than the average American; 13% had worse depression; and overall, about half of CLL patients reported moderate or severe cancer-related stress in at least the areas of eating and nutrition at 52%. Forty-two percent reported concerns about physical activity, and 39% of those patients reported worries about the future. And lastly, I wanted to highlight that about 30% of the CLL patients said that the disease affected their relationships with their friends and family, and 24% were concerned about their ability to think clearly due to chemo brain. So, again, these are some of the quality-of-life experiences and cancer-related distress experiences that the respondents in our longitudinal survey reported.

00:26:42

Moderator, RTI International

Thank you for sharing that data, **[Participant 7]**. We appreciate it. And **[Participant 1]**?

00:26:50

Participant 1 (registered as a representative of a patient advocacy organization)

Yeah, I raised my hand late because I wanted to hear all the patients speak first, and so I'll say that **[REDACTED]** experience, very similar, diagnosed early. So, I'll just add a couple of additive things, maybe with my policy hat as well.

You're seeing an inordinate number of people on this call talk about early diagnosis. That's not very typical. The average age of diagnosis is 70. So, we have a heavy Medicare population in CLL, and this is the second drug for CLL being negotiated in two years. And so, the stress level is high in terms of being able to ensure access.

The other thing, because of the younger patients, we're really asking CMS to keep an eye on how your negotiations are impacting commercial pricing, because in the early years, for a lot of these patients, we don't have an out-of-pocket cap. And so, it's really important that there, the medicines remain affordable.

Once you get to Medicare, CLL patients quickly get to their out-of-pocket cap. So, the negotiation is important. But it's not as relevant on patients' pocketbooks as you might think, because mostly all cancers really are going to hit that out-of-pocket cap. So, the effect on access and innovation is really the critical pieces. From what **[REDACTED]** mentioned in her opening remarks there.

And the other thing I would say, you heard a lot from these folks about off-label need of medicines, or before they're labeled for those things. And so just to please be aware that all are substantially all that requirement in Part D to cover oncology medicines is so important for this community because it's not just access to Calquence. It's all these others, as everyone has mentioned, that keep it chronic. And so that's really important for the future.

00:28:42
Moderator, RTI International

Thank you, **[Participant 1]**, and we'll definitely get into some of those issues more later on. I appreciate the comments. Okay, before we move on, I just want to ask for clarification really quick. So, does anyone here feel that they can offer experiences related to mantle cell lymphoma? I just wanted to clarify. Otherwise, I'll be focusing kind of more exclusively on CLL and SLL.

00:29:07
Participant 1 (registered as a representative of a patient advocacy organization)

[MODERATOR], I should have offered that CLL Society has organized a rare cancer coalition, and if you want us to follow up with you afterwards, we're happy to help you reach the mantle cell perspective through that coalition.

00:29:21
Moderator, RTI International

Thank you, **[Participant 1]**. Okay, so, hearing none, I'm gonna focus on the CLL and SLL. Thank you. Thank you for letting me clarify that really quick.

Okay, now, let's talk about what aspects of CLL or SLL are most important to patients to have managed or treated. And if you want to just raise your hands like last time or jump in, either way is fine.

00:29:49
Participant 1 (registered as a representative of a patient advocacy organization)

Sorry you asked what aspects are most important to manage? Okay.

00:29:54
Moderator, RTI International

Yeah, what aspects of the condition are most important to have managed or treated? These could be things such as how you feel, function in daily life, how long you live, that type of thing. **[Participant 6]?**

00:30:10
Participant 6 (registered as a patient)

Think not just for me, but I suspect for everyone, managing the fatigue is the biggest problem. There are so many other, you could blame old age, as has been pointed out, most of the people when they're diagnosed with CLL are in their seventies. And so, okay, is the fatigue due to the fact that we're in our seventies? Or is it due to the impact of CLL? I would vote that as the biggest thing that needs to be managed, the fatigue.

00:30:49
Moderator, RTI International

Okay. Fatigue. Thank you, **[Participant 6]**. What about you, **[Participant 5]**?

00:30:55

Participant 5 (registered as a patient)

I think there's a whole piece of this puzzle that's missing, and that's the mental aspect of having an incurable cancer. I think that when you're told initially that you have cancer, they tell you it's incurable. They also tell you, a lot of times initially, we're not going to do anything about it, because we're going to put you in a period of watch and wait, which can be devastating to patients because they know if you have cancer, you do something about it. But unfortunately, with CLL, that's not always the case. And you go through periods of possibly long times where you're not needing treatment, but it's like a roller coaster where you can go for no treatment for a period of time. Then you have treatment. You respond to treatment for a period of time. But then it comes back, and you go through the whole cycle again.

So I think there's always this cloud over patients' heads that eventually, I'm going to need treatment again. I don't know when everybody, the way that people find out a lot of times about their CLL, as was mentioned before, is just through routine blood tests, and even through relapses, sometimes you don't feel any different, but then the doctor comes back and tells you, oh, your blood tests are indicating that you're progressing again. So, I think the mental aspect of dealing with this, and then not maybe knowing what your next options might be is huge. And that's why the ability to have multiple options for patients when time comes for treatment, kind of relieves that, that they can figure out, oh, I know what my next step might be, but again, I think the mental side of this is sometimes pushed to the side.

00:32:53

Moderator, RTI International

Got it. Okay. Fatigue, mental health impacts. **[Participant 4]**?

00:32:59

Participant 4 (registered as a patient and representative of a patient advocacy organization)

Let me just add some meat to what was said, and then add a different topic. In terms of our study, we did the largest study ever of CLL patients that was presented at ASH about 1,100 patients, and found that most patients, a vast number of patients were asymptomatic at the time of diagnosis, but after the diagnosis the majority had anxiety. Anxiety was the big issue, much bigger issue than depression. Fatigue is the most common symptom that we see in CLL. And the living with the uncertainty, I think, is a part of both the fatigue and the anxiety.

I think the one thing that was mentioned by **[Participant 6]** but is really a big issue that's happened since in the last several years with the pandemic is it's really peeled the cover off the fact that we're immunocompromised. And the funerals and memorial services that I and my friends have been attending aren't for people dying of CLL now, thank goodness, but of complications of CLL. Infectious complications, not just COVID, but pneumonia and other infections, and also second malignancies, because the immune system, of course, keeps the second malignancies down. So, people are dying of second cancers, prostate colon cancer, lung cancer, melanoma, ovarian cancer.

Reconstituting the immune system is a screaming unmet need in CLL. So, there's also a fear that as we're surviving longer and longer, not only are we developing second malignancies, there's a couple that really scare us. The malignancies, one is Richter's transformation, which happens five to 10% of patients for which there is no therapies available. So, every time we get a blood test or scan,

we're worried that we have Richter's, and that's essentially a death sentence at this point, for... there are wonderful exceptions, but they are exceptions.

So, and the other is myelodysplastic syndromes, which seem to be reduced because of the drugs we have, like the BTKis, and the very early evidence that the lack of chemo seems to be reducing the incidence of myelodysplastic syndromes. So, those are good things.

The last, a couple other symptoms that I had, and I think others have had that aren't, that don't sound that major, is that some of us get pretty unsightly, uncomfortable lymph nodes. I mean, I had to grow a big Santa Claus beard, hide it, and I work as a **[REDACTED]**. My patients were often more worried about, are you okay, **[Participant 4]**? You look kind of funny, what's going on with you and having every time you walk into a place, explain what's going on with you, why you look like a chipmunk. I mean, it can be pretty devastating that and enlarged spleen. I had a massively enlarged spleen. You can feel full. You can feel heavy. You can't eat properly, and none of these are life-threatening symptoms, but they're certainly annoying symptoms that are an issue.

And also the disease itself can lead to the problems that I talked about, about platelets, anemia, which in itself have a whole other set of symptoms that are associated with that, that's not uncommon. But the immunocompromised has really become a major issue. I hope you could hear me better this time. Yeah.

00:36:41

Moderator, RTI International

I can. I hope others can as well. Okay, thank you, **[Participant 4]**, for sharing about those immune system concerns as well as those other troublesome symptoms. I do want to give everybody a heads up. I'm going to turn to **[Participant 2]**, **[Participant 7],** and **[Participant 3]** really quickly, but I do want to move on and talk in more depth about Calquence soon. So, I just want to remind you, you can always enter comments that you don't get a chance to say out loud into the chat as needed.

Okay, I saw some hands go down. **[Participant 3]**, let me turn to you.

00:37:14

Participant 3 (registered as a representative of a patient advocacy organization)

Yeah, no, just very quickly. I just want to kind of echo what **[Participant 4]** said about the immunocompromised. [B]eing in my early sixties I'm at a point where I'm looking to travel a lot, to do a lot of different things. And I know a lot of other people around my age, very active. And it's the number one question I hear from people is, what can I do? Is it safe for me to do this? Can I fly? Can I go to a concert? Can I go to the opera?

And for people who don't want to change their lives and still do things, there's definitely a higher level of anxiety as a result of that. So, I think that whole... and it is potentially, and when we know this, more people die from these secondary infections than from the disease itself. So, we know as CLL patients that there's a significant risk involved in that.

00:38:11

Moderator, RTI International

Thank you, **[Participant 3]**, for those comments. **[Participant 2]**?

00:38:14

Participant 2 (registered as a patient)

Yeah, I won't take up too much time, but I just want to reiterate the degree of fatigue. When I was diagnosed, I was relatively young. I had a very dynamic life, burning a candle at both ends, and slowly, it was like I was walking through molasses, and because nothing had happened, and my labs were normal, nobody thought anything of it until I got some imaging, and then that showed the enlarged lymph nodes.

My lymph nodes were uncomfortable. They were painful in my neck, but the fatigue is to the degree that I would say I would make a salad, but then I couldn't, didn't have the energy to chew it, and that's the degree of debilitating fatigue, and my dynamic life is completely changed now because of this disease. It was well-controlled with Calquence. So, I'm very appreciative of that. But I do have the anxiety of knowing, and I'm a single person. I've been doing cancer by myself. So, it's very challenging, financially and logistically. When I get that fatigued, it's like, how can I manage a life and an apartment and a car and taxes and all the things that we need to do when I'm on my own with that degree of fatigue. So, I just wanted to stress that it is life-altering fatigue for some of us.

00:39:35

Moderator, RTI International

Thank you for sharing that, **[Participant 2]**. I appreciate it. Okay, and I appreciate everybody sharing the experiences we've heard about so far. I'm going to switch gears a little bit. And now we're going to focus on talking about your experiences and the experiences of patients in general with Calquence. In addition to Calquence, I do want to note that we also want to hear about experiences related to other medications that are similar to Calquence for CLL and SLL.

Sometimes we refer to these drugs used to treat the same condition or symptoms as therapeutic alternatives. So, you may hear me use that term. So, when considering potential medications for CLL or SLL, what matters to patients the most? What features of the medication matter the most? **[Participant 3]**?

00:40:32

Participant 3 (registered as a representative of a patient advocacy)

Yeah. So, again, my perspective being at the early stage of this, but looking out and my thought is, how am I going to get through the next 30 years. [A]re there enough treatments? [H]ow do I structure a treatment regimen over a period of time like that? So, for me, and again, this is just my perspective, it's not as much about each individual treatment. But what's the order? [F]or example, the venetoclax and obinutuzumab tends to be a little bit harder for a lot of people to tolerate. So, do I want to start with that while I'm younger and healthier and move on to something like a BTK inhibitor long term at a later date? So, it's really looking at all of the available treatments and saying, what do I do first? What's my best option for structuring, so that I know I can live the next 30 years of my life?

And along with that, obviously is the incredible need for continued innovation, because, and just looking at some of the trials that are going on right now, where we're looking at not just Calquence from a long term, take it till it stops being effective perspective. But is there a way to combine Calquence with another drug so that it can be a limited duration, one year or two years and still have the same effect? So, that's where I'm sort of focusing my mental effort at this point, is trying to

figure out what's out there? What makes the most sense? What are the side effects of each? And how do I adjust my life so that I can create a treatment regimen that works.

00:42:24

Moderator, RTI International

Thank you for sharing that, **[Participant 3]**. That's helpful to understand, and we'll definitely have time to delve deeper into the benefits and drawbacks of Calquence and alternative therapies. Okay, I'm gonna turn to **[Participant 5]**.

00:42:39

Participant 5 (registered as a patient)

I think **[Participant 3]** hit on a little bit, but sequencing of drugs is really important for the long term. If you know that typically the drugs will last for so long. And then you have to move to something else. But I think when patients look at treatment, they look at quality of life with how am I going to feel when I take this drug?

And then another option is, how long do I have to take this drug? [T]ypically, the BTK inhibitors are a drug that you take until you can no longer tolerate it, or until you progress, which could be years. All told, I was on a BTK inhibitor for nine and a half years. So, for me, it was a long time on this particular drug.

But other people would rather be on a more fixed duration treatment where they can take a drug for maybe a year or combination of drugs per year, and then they're done, and that's their mindset. They would just like to say, hey, I'd like to get this over, and I think patients are becoming more educated in terms of what the pros and cons of each approach are. And I think in some cases it's a personal choice that they say, I don't mind taking a pill every day to manage my disease, and hopefully that'll last for a long time. But I think **[Participant 3]** hit on a very important point that the new trials that are out there that are using combinations of drugs together is really showing some great promise in CLL patients. And I think that going forward that's going to be a major, major game changer for patients, especially for those in the first line setting.

00:44:23

Moderator, RTI International

Thank you. **[Participant 5]**. Okay, **[Participant 6]**?

00:44:27

Participant 6 (registered as a patient)

Let me sort of summarize and elaborate when we're trying to figure out whether to take Calquence or zanabrutinib or Ibrutinib, etc., essentially, CLL patients are dealing with a three-dimensional problem among side effects, effectiveness, timing. Depending on our age, our side effect profile, etc., we now have the option of working with our docs to figure out which alternative or combination best meets that three-dimensional problem because we all end up grappling with that. In my case I didn't have lots of options like **[Participant 4]**, only Ibrutinib was available at the time I needed it. Now it's a different situation, and my HEMOC [hematologist oncologist] and I have worked through a schedule where, over the next six years, I'll be taking A and B, and when they fail, take C and D.

I didn't have a B, I didn't have B, C, and D 15 years ago. So I, I think the key detail now is understanding that there's this three-dimensional problem that we all have to grapple with. And

sometimes it's trial and error. We try one. And if the side effects become a problem, then we go to the next one and the next one, and that's where we're at.

00:46:12
Moderator, RTI International

Thank you, **[Participant 6]**, for sharing that. Okay, **[Participant 2]**?

00:46:17
Participant 2 (registered as a patient)

Yeah. The sequencing of what would be the next treatment is always, I think, in the back of our minds. And will that treatment work for me? Will the side effects be tolerable? So, there's that constant level of stress. Will I be able to afford the next treatment? Will it be effective for me, and how long will it be effective for me? And can I manage the side effects? So, those are always the things that are roiling in the back of our minds as we're going along trying to live life as normally as possible. So, just to reinforce what everyone else said, having options, because not every drug is effective or well tolerated by each patient.

00:46:59
Moderator, RTI International

Thank you. **[Participant 2]**. And **[Participant 4]**, I'm gonna turn to you next. But I'm gonna ask for you to keep it kind of brief, because I want to move into talking about the benefits and drawbacks specific to Calquence in a moment.

00:47:11
Participant 4 (registered as a patient and representative of a patient advocacy organization)

Absolutely. So, I think what you heard is it's going to be different at different ages, and the needs of a 40- or 50-year-old diagnosed with CLL are going to be very different than a 70- or 80-year-old. That said, across the board, what patients are interested in, is does this drug work? What's my progression-free survival? What's my overall survival? That's critical to patients. And then, what's the adverse event profile? Can I afford the drug? How long will I be taking it?

00:47:41
Moderator, RTI International

Thank you, **[Participant 4].** Okay, considering patients' experiences with Calquence for CLL and SLL, what are the main benefits that you or patients in general experience with taking Calquence? What do folks like about Calquence?

All right, **[Participant 7]**, since I didn't get to hear from you last time? Let me turn to you now.

00:48:06
Participant 7 (registered as a representative of a patient advocacy organization)

Yes. Can you hear me? Okay.

00:48:08
Moderator, RTI International

Yeah, right.

00:48:09

Participant 7 (registered as a representative of a patient advocacy organization)

Okay, wonderful. So, we looked at, looking at Calquence, the therapeutic alternatives we looked at were ibrutinid, zanubrutinib, and the combination of Venclexta and Gazyva, and what we found from our academic medical advisor is that ibrutinid or Ambrovica, they tell us that they're really moving away from starting that for new patients on that drug. But they're keeping patients for whom it seems to be working on that drug.

And what we found when it looked at side effects, and the benefits is that Calquence has fairly similar side effects for blood cancer treatment. But when you compare it to Brukinsa, Calquence had lower risk of side effects like hypertension and hemorrhage, and while there aren't any head-to-head studies comparing the combination of Calquence and Gazyva and Venclexta and Gazyva, our evidence from separate trials seems to suggest that the Venclexta combination has more side effects related to neutropenia and tumor lysis syndrome, but, and those can be problems for older patients with renal problems and patients who live far from a treatment center. But the biggest difference in the patient experience that we heard, and that we learned between the Calquence, Gazyva combination and the Venclexta, Gazyva combination is that the Calquence, Gazyva combination is given indefinitely, while the latter is a fixed duration therapy that only takes 12 months, and that has important implications for patients, quality of life and costs, where for a chronic blood cancer patient, they may have significant time without having to be on therapy, and from the results that we heard from patients in the survey that really means a lot to them, and is a very important factor for them when they consider treatment. And then there are some studies that do show that significantly lower healthcare costs after 12 months of therapy ends, that patients really value that. And so that's just kind of underscoring what I think some of the patients have shared here about their experience, about affordability, and about what they really value. And so that was just some data that I wanted to share, that I think can really help supplement and complement what you're hearing as well.

00:50:37

Moderator, RTI International

Thank you, **[Participant 7]**, again for, for incorporating that data into our conversation. It's helpful. All right, **[Participant 2]**?

00:50:44

Participant 2 (registered as a patient)

Yes, I really thought that treatment was going to be really disruptive to my life, and I found with Calquence, taking the capsule twice a day, it was so easy to incorporate into my life with my other supplements and things that I was taking throughout the day. So, there was no inconvenience for having to go for infusions and that sort of thing. I was in a clinical trial, so I was watching more closely. There were appointments, more appointments and labs and things, but the ease of taking Calquence and the lack of serious side effects for me, I would have stayed on that drug forever, if need be, and if it was effective for me. So, it's just very easy to incorporate into one's life, and I had a busy life, and I am, as I said, doing everything on my own. So, the ease of treatment was really important, and Calquence was great for that.

00:51:47

Moderator, RTI International

Thank you, **[Participant 2]**. Ease of use. Convenient. Yep.

00:51:51

Participant 1 (registered as a representative of a patient advocacy organization)

I'm going to pick you up on your offer to jump in, just to say before **[Participant 4]**, just to say that the other piece of that, that **[Participant 2]** is mentioning is that it also helps immune-compromised patients avoid places where their immune compromise could lead to life-threatening consequences about being able to take it at home, so that I just wanted to add that point.

00:52:13

Moderator, RTI International

Thank you for that addition, **[Participant 1]**. **[Participant 4]**?

00:52:18

Participant 4 (registered as a representative of a patient advocacy organization)

When I started on Ibrutinib we didn't know the adverse event profile, and the things that, the day-to-day stuff, the muscle aches and pains, the myalgias, those kinds of things were just incredibly annoying. I didn't have any other options, so I just stuck with it. But nowadays we have clear evidence that the second generation of BTK inhibitors, acalabrutinib, zanubrutinib, and if you want to add pirtobrutinib to that, are much better tolerated and have less off-target effects, so I think on a day-to-day basis that makes a huge difference. One of the other big differences that we know now is that the risk of sudden death, which is the adverse event profile that none of us want, while small with Ibrutinib, about 1%, is negligible with the others. Also, the cardiac adverse events are much lower with the second generation, and a lot of us are older, and already have a risk of hypertension and have a risk of atrial fibrillation and other cardiac issues. So, generally, acalabrutinib is in our experience with our patient community is extremely well tolerated. There are headaches at the beginning, but most patients get through that. But other than the headaches at the beginning, which are annoying for a lot of patients, and that's a very time-limited therapy that usually Tylenol and caffeine will take care of, it's really a non-event like **[Participant 2]** described for most patients. They're remarkably surprised. And a lot of people say, this is kind of I'm back to my old self again when I start taking these medications.

00:54:04

Moderator, RTI International

Thank you, **[Participant 4]**, and now I've already heard about some side effects. But I'd like to hear about other drawbacks or challenges that patients experience with Calquence. What do you wish was different about Calquence? If anything?

Okay, back to you, **[Participant 4]**.

00:54:27

Participant 4 (registered as a representative of a patient advocacy organization)

I think the new formulation that for a while you couldn't take it with a proton pump inhibitor, and again, that was a big problem. But the new formulation has solved that issue. That was a significant

issue for a lot of patients. [T]here's a little limiting in the dosing. Some people do have some intolerance, so you could take it, or you take half of it, or you don't take it. Other drugs you can have a little more play in how much of the pills you take. That's a minor inconvenience with it, but it can be, for some people who are intolerant, or have a low body mass, so that can be an issue.

00:55:12

Moderator, RTI International

Thank you, **[Participant 4]**. Other major drawbacks or challenges associated with Calquence?

00:55:19

Participant 2 (registered as a patient)

I'll jump on what **[Participant 4]** said. That was the reason I had to stop Calquence, is that I needed PPI [proton pump inhibitor] for acid reflux. I needed that. So, after being five years on treatment, I had to stop because of that reason. But in that timeframe the tablet was created where you could take PPIs, but because it was a clinical trial and I was in remission, we just decided to leave it at that. So otherwise, as I said, I would have stayed on that drug, mild bruising, some petechia, easy bleeding, but all of that was certainly manageable.

00:55:58

Moderator, RTI International

Thank you, **[Participant 2]**. Okay, I've heard you all mention some of the other medications that you've taken over time, but for any that I haven't heard yet, I'm wondering what other medications beyond Calquence you or your loved ones have taken, whether currently or in the past, to treat CLL or SLL. **[Participant 5]**?

Oh, **[Participant 5]**, you're still on mute. Oh, **[Participant 5]**, could you unmute yourself?

Thanks.

00:56:33

Participant 5 (registered as a patient)

Okay. I was originally treated with chemotherapy, and the second round I was treated with monoclonal antibody and high dose methylprednisolone. Then I was on chemotherapy again, and then I started on the clinical trial for Ibrutinib, which I was on for about nine and a half years, four and a half years as a single agent. But we added venetoclax to it after about four and a half years.

At that point in time, I got to undetectable, unmeasurable disease. They could not find any CLL. And an interesting point here is that I had been in that state for about 19 months, and it was December of the year, and we made a conscious decision to stop the treatment because we couldn't find any CLL. But one of the main considerations for stopping treatment was in January, I was going to have to pay the copay for the venetoclax, which, an annual basis for me at that time, before the limits were put on, it was $12,500. So, for me it was a conscious decision, to not pay that money. I was doing well, so, we kind of said, okay, this may be a good time to stop.

It turned out it was not the correct decision. Four months later I relapsed, and then I had to pay the out-of-pocket expense, anyway. So, I've been on a lot of drugs. I moved to a third or fourth generation BTK inhibitor called pirtobrutinib, which works after you might have developed a mutation on one of the original three BTK inhibitors. And currently, I'm on that, and my CLL is under control.

But we're always looking at, what next? Because I'm assuming based on, I have all the bad markers, just like **[Participant 4]** said. Just like **[Participant 6]** said. Technically, I should not be here, 25 years later after diagnosis, but it's only because of the fact that these drugs have been created over the time that I've had CLL, that I'm here today. I mean, I can honestly say that I would not be here unless these drugs were available to me, and different versions of the same class of drug where one version did not work, the second version did work. So, I think having options for patients, again, is so important, even though you may have issues with a particular drug, it may just be an adverse event with that drug. And if you move to another drug in that same class, it may work for you.

So, that's why options are so important for CLL patients.

00:59:36

Moderator, RTI International

Thank you, **[Participant 5]**. **[Participant 4]**?

00:59:39

Participant 4 (registered as a representative of a patient advocacy organization)

So, I mentioned that I was on Ibrutinib. I've also been on a number of immunotherapies. I've been on rituximab, which is a lot like obinutuzumab or Gazyva, an earlier generation of that.

I'm also now on epcoritamab, which is a bispecific T-cell engager, which is experimental, and I've also had CAR-T therapy, which is a cellular immune therapy, which is experimental, but now is approved in CLL.

The other drug that I was on, and this is, I would push, though this isn't particularly the topic right now, is to have access to drugs off-label because I was on a drug that is not used to treat CLL, but has some literature that it could, and back in 2006 and 7, there was no other options. I was on Cyclosporine, which is used for people who are ejecting or... transplanted organs. It's immunosuppressive. But there were some papers that showed it had activity in CLL, and when it was used to treat my ITP, lo and behold, it got me into remission for CLL. Nobody really expected that, but I took it and ran with it. The last thing I point out is, I had a bone marrow transplant, which is still kind of the hail Mary pass in CLL, but still an option that patients need.

01:00:52

Moderator, RTI International

Thank you, **[Participant 4]**. And I'm going to turn to you, **[Participant 1]**, real quick before we talk a little bit about how the benefits and drawbacks of these other medications compare to Calquence.

Oh, **[Participant 1]**, you're on mute.

01:01:07

Participant 1 (registered as a representative of a patient advocacy organization)

I think this is an important time to point out that yesterday the administration said it intends to implement a system of parity between small molecules and biologics for innovation. You're hearing so much from all these patients about the need for continued innovation to keep this a chronic condition. We're lucky to have CLL on this label. But imagine if our nine years had run out when the company was still studying CLL and the mantle cell as a combination therapy, which was previously reserved as a monotherapy for later lines of treatment, that was approved as first line, literally days before the last administration selected this drug. So, I think, as you hear **[Participant 4]** talk about

off label, I wanted to just add that point that it's really important to think about how what you're doing is going to impact our ability to continue getting both on- and off-label treatment, and that things continue to be added on to label like CLL, which was just literally, as I said, a month before, the drug was selected by the last administration.

And it's still being studied in GVHD [Graft-versus-host disease] for example. So, there's also non-cancer, but very rare conditions for which this drug is being researched. And we brought that up last year with CMS. Because Imbruvica had the same thing. But this has a better tolerability profile, as you just heard other people say, which is really important for the GVHD patients, too.

01:02:40

Moderator, RTI International

Thank you, **[Participant 1]**, for sharing those comments. Okay, we're going to switch gears momentarily. But before we do, and you all have already gotten into this a bit, but how do the benefits and drawbacks of these other medications differ from Calquence, if at all? Again, I know that you've covered this a little bit, but any other important differences? Okay, **[Participant 4]**?

01:03:07

Participant 4 (registered as a patient and representative of a patient advocacy organization)

I can start. I mean, while it's not a primary factor, I'd be lying to say that an oral medication, patients are going to always prefer over an IV [intravenous] medication.

The second is that it's a real easy medicine to start, and a relatively easy medicine to stop, and, unlike venetoclax, which involves a risk of tumor lysis and a ramp up to prevent that, close monitoring so patients need to be close to that. Also, it's used in combination also with an IV drug, which can be a problem. The fact that it's extremely well tolerated compared to the other BTK, especially compared to Ibrutinib, also is a significant advantage for it.

The other therapies that we talked about that are approved in CLL are much more onerous for the patients in much higher risk, like CAR-T therapy and a bone marrow transplant are much more difficult therapies for patients to go through the ability right now for patients to get acalabrutinib in combination with venetoclax based on the NCCN [National Comprehensive Cancer Network] guidelines is an increasingly attractive option for some patients, because it gives the advantage of those two wonderful oral drugs and all oral therapy that's time limited and seems extraordinarily effective. I don't think it'll be the last of the all oral combinations. I think it'll be the first, but it's something that our community is very excited about.

01:04:41

Moderator, RTI International

Thank you for sharing that, **[Participant 4]**. And **[Participant 7]**, real quick. And then we're gonna switch here.

01:04:45

Participant 7 (registered as a representative of a patient advocacy organization)

Yes, so I just wanna say, I just, I think **[Participant 1]** did a great job and **[Participant 4]**, as well, and talking about some of the benefits of oral cancer therapies. And so, I just put in the chat, it was just basically like a plus one for what they said.

01:05:03

Moderator, RTI International

Thank you, and I just want to put another plug in for the chat just in general. Please don't hesitate to add comments there, if we don't have time to talk about them out loud. Okay.

Well, like I said, switching gears a little bit. So, again, thank you so much for all the helpful input you've provided so far. Now, I want to talk a little bit about how Calquence and other medications for CLL or SLL meet patients' needs.

What would it be like for someone who has CLL or SLL if Calquence, or other medications for this condition, were not available? In other words, what needs associated with CLL or SLL does Calquence or other medications for this condition meet?

All right. Turning to you again, **[Participant 4]**.

01:05:54

Participant 4 (registered as a representative of a patient advocacy organization)

Well, I'll start for a number of us with bad prognostic markers, we're chemo refractory and until there was drugs in the BTK class and now the Bcl-2 class CLL with 17p deletion or TP53 aberrant disease had a terrible prognosis. It was really a death sentence, so the reality, I mean, the big thing is that it was the breakthrough in the BTK inhibitors. And now the improvement with a drug like acalabrutinib that are keeping us alive.

That's the unmet need for these, if it wasn't for if I'd been born two or three years earlier, I wouldn't be here. If I'd been born two or three years later, I never would have had a bone marrow transplant, gone through all the stuff that I went through. So, these drugs are lifesaving, especially for the percentage of patients. And the studies have shown that patients who have this refractory disease, it may only be five to 10% at the time of diagnosis, but it's up to 50% at the time of relapse. So, the therapy select for this, and then we certainly need these drugs as a second line therapy. So, for me, these drugs are existentially save, these are lifesaving medications. That's not overstating it.

01:07:21

Moderator, RTI International

Thank you, **[Participant 4]**. **[Participant 5]**, I had seen your hand next.

01:07:26

Participant 5 (registered as a patient)

I'll be very blunt. I would not be alive today without these medicines, because there were no options for me. I became chemo refractory, which meant there were no conventional treatments. I would have had to have a bone marrow transplant, which **[Participant 4]** had, and when they talked to me about that, they said, 25% of the people never get out of the hospital after a transplant, which didn't sound very appealing to me. So, flat out. Without these treatments, I would not be alive today.

01:07:57

Moderator, RTI International

Thank you, **[Participant 5]**, for sharing that. **[Participant 3]**, we haven't heard from you in a bit.

01:08:03

Participant 3 (registered as a representative of a patient advocacy organization)

Sorry I had to log off for a minute, my keyboard and mouse decided they weren't going to cooperate.

So, yeah, at the risk of being a little bit repetitive. I think to me it's just that, it goes back to the sequencing. [I]f I'm looking at surviving another 30 years with this disease, it's not enough for me to have one treatment. Now with my biomarkers, I probably will respond well to just about any of the therapies that are available, including chemo, if that were my only option. But there's nothing available to me right now that as a single treatment could sustain me for 30 years. So, whatever I choose to do first, second, and third, it's all about having enough options in that sequence, and quite honestly, I mean I would hope that at some point we'll start talking about Calquence as a second line therapy.

Maybe in the next five years, something will come along that's that much better, that sort of dominates as a first line therapy. So, I just think that we need to continue that innovation and make sure. And I'll add just one more point on the idea of longevity. I spend a lot of time looking at groups like Reddit, online groups that tend to cater to younger audiences. And although we know that the average age of this, people being diagnosed with this disease is about 70, it's amazing how many people I read about who are in their thirties, forties, and fifties who are being diagnosed so, and I don't know if that's increasing. I have no data to show if it's more now than it was 10 or 20 years ago. But, those are people who are looking at not only living 20 or 30 years with this disease, but possibly 40 or 50. So, it just makes the need for innovation that much stronger.

01:10:06

Moderator, RTI International

Thank you, **[Participant 3]**. I'm glad those tech issues are sorted. **[Participant 1]**?

01:10:11

Participant 1 (registered as a representative of a patient advocacy organization)

Yeah, you're asking the same question in different ways, I feel like. [W]hat would it be to live without this treatment, after the question about, what are the benefits. I just want to make sure that we have a moment to say that the negotiations when we pointed out last year with Imbruvica that, hey, if you select Calquence, you will put at risk being able to get that CLL indication on the label. And now by having chosen it, you put at risk the GVHD research ever making it to label. And now what **[Participant 3]** is saying, you put at risk where your negotiation goes in terms of what it will be priced at in the private commercial market where patients don't have this cap.

These things are really important to this community. You're not hearing people on this call tell you that Calquence is the be-all, end-all. You're hearing them say to you, the sequence is what is the be-all, end-all. And the fact that all these drugs need to be available to patients is critical. So, **[REDACTED]**, for example, ended up already with an insurance-related problem that I suspect is fairly common. Like most cancer treatments it's relatively costly. So, access is an issue with prior authorization.

She was, after a year, where all her medical records indicated that she was doing incredibly well, and it was keeping her alive. The insurance company decided to stop providing it, and it took repeated appeals and appeals and appeals, and even mediation, to get her back on it, by which time she had missed doses. So, fast forward to a negotiated environment where it's really important for CMS to understand, hey, they have a prior auth, but that's it, no big deal. No, it's the paperwork

and hassle and everything that comes behind that prior auth, that'll be really important for CMS to track here, and to make sure they're tracking it for all the other treatments as well. Because, again, it's the sequence that really matters. If this drug had been negotiated 13 years instead of nine years from its start, we might be at a place where we would have gotten GVHD on the label, and that is being put at risk, and I know when new things go on label CMS can renegotiate. But I don't see an environment where you'll renegotiate the price up.

And so, really, watching these incentives and disincentives from this negotiation is really critical for our community.

01:12:40

Moderator, RTI International

Thank you for that input, **[Participant 1]**. Okay, and this is kind of the flip side of that previous question, what aspects, if any, of CLL or SLL are Calquence or other medications for this condition currently unable to address? I know we've talked a little bit about innovation and clinical trials, what is not currently being addressed by the medications that are available? [Participant 4]?

01:13:14

Participant 4 (registered as a patient and representative of a patient advocacy organization)

Well, I think the first obvious is, we don't have any curative therapies outside of the occasional patient with the transplant. We have no curative therapies. I think we have a hint that some of these combinations that are coming may have functional cures. I mean, if you've got kind of a flat line in terms of progression on the Kaplan-Meier curves for 5, 6, 7, 8 years. It's not enough to say it's cured, but it's certainly a hint that things might be good. The other is reconstituting the immune system that we talked about. We don't have an answer for that.

The third, and we've talked a lot about, this is the sequencing. I like to call it the chess game. We don't know what the best therapy is to use first. How, if you use venetoclax first, and then go to acala[brutinib]. Is that the way to go? Or should you do acala[brutinib] first, and then ven[etoclax]? Or should you use a combo first? Should you sequence? Should you do parallel?

These are trials that are going to be very difficult to do. In fact, we're almost a victim of our own success. The fact that we're doing well, these trials could take years and years because there's great rescues available. There's great front line. There's great second line. When we get to third line, it gets a little thinner, a little iffier and stuff like that. But a lot of us are getting to third, and like, you're seeing around this table. A lot of us are getting to third and fourth and fifth lines in terms of what our therapies are. But I think if the, what we look for in CLL Society, we sponsor research and those unmet needs are reconstituting the immune system, potentially curative therapies, double refractory disease, people who fail the BTK and Bcl-2 and Richter's transformation. Those are the unmet needs. Acala helps us with those, but it doesn't solve any of those.

01:14:59

Moderator, RTI International

Thank you, **[Participant 4]**. **[Participant 6]**?

01:15:06

Participant 6 (registered as a patient)

When **[Participant 4]** talked about the immune system issues that are not really helped, in fact, they're made worse by acalabrutinib. Let me tell you about how bad that situation gets. My immune system, and others with CLL has been so damaged that we're doing subcutaneous gamma globulin infusions at home. Once a week I stick four needles into my gut and sit for two hours while gamma globulin is pumped into me to protect me from all the bad stuff that happens when you have an immune system problem, pneumonia, etc. That's a perfect example of something that has to be done because of the failure of all the BTKs. Their effectiveness is based on damaging our immune system essentially, because the B-cells get damaged.

01:16:11

Moderator, RTI International

Thank you, **[Participant 6]**. Okay, thanks again, for everybody's input. As we get close to the end of today's discussion, I want to wrap things up by talking about your perceptions of the overall importance of Calquence to patients. So, thinking about the different topics that we discussed today, how would you summarize the importance of Calquence for people with CLL or SLL? **[Participant 1]**?

01:16:42

Participant 1 (registered as a representative of a patient advocacy organization)

I think the really important things for CMS to be thinking about with Calquence is making sure that future innovation can continue to happen. There are combinations, for example, that we talked about already, that have yet to be studied. I think it's really important for CMS to think about the commercial price implications of what we do here. I think it's important for CMS to think about your ability to still move this product to 13 years instead of nine under current statute, which is allowed, because you only had to choose up to 15 in this round of negotiations.

I think it's also really important to think about NCCN guidelines and off-label uses of this treatment. And I think it's important to think about off-label uses that are not even cancer related like I mentioned before, that will no longer get studied.

01:17:39

Moderator, RTI International

Thank you, **[Participant 1]**. **[Participant 3]**?

01:17:43

Participant 3 (registered as a representative of a patient advocacy organization)

Yeah, I think if to summarize, it's lifesaving, I mean, that's the easiest way to put it. There are, if you take this drug and more broadly, BTK inhibitors out of the equation, people with CLL simply won't live as long or have the same hope for a normal length life.

So, they're truly lifesaving drugs, despite all of the drawbacks, despite the issues, despite the fact that they don't work for everyone. They save a lot of lives.

01:18:21

Moderator, RTI International

Thank you, **[Participant 3]**. **[Participant 4]**?

01:18:25

Participant 4 (registered as a representative of a patient advocacy organization)

I'm going to pull a couple things together. We started with the fact that when you know one CLL patient, you know one CLL patient, and it's a tremendously heterogeneous disease. And there's people who've lived 60 years and never needed treatment. And people who are, the day they're diagnosed, they're on therapy and lots in between. So, you add that to the fact that different drugs work differently for different people. You cannot make these drugs difficult. Acalabrutinib is a lifesaver for a lot of patients, not for all patients, but for a lot of patients. It should be an option. [P]eople shouldn't have to go through what **[REDACTED]** went through, and that is not an unusual story, and doctors don't... **[REDACTED]**. A prior authorization is a pain to deal with. I could use more colorful language, and it doesn't always happen. And then I've got to arrange a time to talk with another physician, who probably doesn't see any CLL, I mean, it's the whole system.

Sometimes I'm talking to an ophthalmologist about a hematological disorder. I mean, I'm not making this stuff up. And that person is making a decision about the patient in front of me. So, we need to avoid these step edits. We need to avoid the difficulties of prior authorization. There's all kinds of backdoor ways that health systems... and I know this is beyond CMS' care. But what happens at CMS influences what happens in commercial insurance and what happens in Medicare plus and whether things are on formulary, and don't even get me started on pharmacy benefit managers, and how that kicks in, and sometimes a profit motive seems more important than taking care of the patient in front of you. So, I think you have to think about the implications of these things when you're making decisions on lifesaving drugs.

01:20:15

Moderator, RTI International

Thanks, **[Participant 4]**. **[Participant 7]**?

01:20:20

Participant 7 (registered as a representative of a patient advocacy organization)

Thank you. So, I wanted to just underscore and reiterate what others have said so eloquently. It's just what the importance of innovation means, and the importance of having multiple alternative treatments and access. I believe someone, I think it was **[Participant 5]** who said earlier, at a certain point, the medication might stop working, and you need something else, another alternative out there. And so, it's lifesaving, life-enhancing, life-preserving.

I also wanted to talk about, just to dig a little bit more, like what Calquence means. We know it's so important, and it's lifesaving, life-enhancing, life-preserving. But we also know that the financial burden is significant for many patients. I always want to go back when I make my comments. [M]y comments are steeped in the research that we have done. And so, our CSC research has found that 29% of patients with CLL or multiple myeloma, so this is blood cancer patients, 29% of those patients actually reported depleting their savings to afford their treatment, and 19% borrowed against or use money from a retirement plan. Right?

So this is critical. [H]aving access to medication that is affordable, and that they can access in a timely manner, because our data also shows that with that affordability, what we call financial toxicity, that translates into patients postponing doctor's appointments, missing follow-up appointments, delaying complementary treatment, and even some postponed psychological counseling due to the financial burden. So, I just want to underscore that because of the significant financial burden of this disease, if the end result of the price negotiation is to make these treatments, the copays and the out-of-pocket costs more affordable to patients, that will be a highly valued outcome.

01:22:16

Moderator, RTI International

Thank you, **[Participant 7]**. Okay, before we start wrapping up today's discussion, I just want to turn to my colleague **[SECONDARY MODERATOR]**, to see if there are any follow-up questions to be posed at this point. Oh, **[SECONDARY MODERATOR]**, you're on mute.

01:22:34

Secondary Moderator, RTI International

No, we don't. Thank you for checking, **[MODERATOR]**.

01:22:36

Moderator, RTI International

Okay. All right, no worries all right and I...

01:22:41

Participant 1 (registered as a representative of a patient advocacy organization)

I'm sorry, **[MODERATOR]**. This is **[Participant 1]**, can I...

01:22:45

Moderator, RTI International

Absolutely.

01:22:45

Participant 1 (registered as a representative of a patient advocacy organization)

I couldn't agree more with **[Participant 7]**'s points about financial toxicity. But I do want to clarify that it's really important for CMS to make clear to patients and families, in cancer, the out-of-pocket cost cap is what prevents the toxicities **[Participant 7]** is talking about. Within a matter of a couple of months, we have hit that. So, this negotiation, it's really important that patients understand that this negotiation is not going to help them with financial toxicity problems. This negotiation doesn't impact their out-of-pocket costs or their copays or anything else. They're going to hit that cap.

And so, what's really meaningfully important to our community in CLL, is that the negotiation not have a negative effect on access and innovation, because financial toxicity has already been addressed before this negotiation even begins. So, understanding how these negotiations impact our families is really critical. I didn't want to leave us on a note of confusion, that these negotiations, in fact, do not help patients in our community. That's already been achieved with the out-of-pocket cost cap. And so, it gives us, if you will, the luxury of worrying about, are we going to be able to get through the prior auths? Are we going to be able to get off-label access? Are we going

to ensure that innovation is preserved by future indications for this drug and for other treatments in CLL?

01:24:28

Moderator. RTI International

Thank you, **[Participant 1]**. **[Participant 6]**?

01:24:33

Participant 6 (registered as a patient)

Just wanna add the detail, an example… I love using spreadsheets. So, I did a calculation of how much society has paid to keep me alive since 2014. Over $870,000 has been, was the total of between Medicare, insurance, out-of-pocket, etc. And I'm looking at… I could be a million-dollar man by the time I go, because I'm going to be starting on new rounds of this stuff, and as **[Participant 1]**'s pointed out, the out-of-pocket cap is basically protecting me from the full impact of being a million-dollar man. It's going to cost society a million dollars to keep me alive by the time I go.

01:25:29

Moderator, RTI International

Quite a number, **[Participant 6]**. Thank you for sharing. **[Participant 4]**?

01:25:33

Participant 4 (registered as a patient and representative of a patient advocacy organization)

Yeah, this is not my area of expertise, but my understanding is that when a drug is approved for just one indication, that may exempt it from the negotiations. But when it becomes multiple, then it's possible to be negotiated. CLL is a rare disorder, but it's one of the more common of the rare disorders. So, our friends with mantle cell, or our friends with related, even rarer Waldenström, and even rarer B-cell lymphomas the chances of those drugs being developed for those diseases after they're developed for CLL, is unlikely. The other way can also happen too. Mantle cell is less indolent, more aggressive. So, often the path to getting these drugs approved has been through mantle cell. We get it approved. Then we get it off label for CLL. So, patients don't have to wait. That pathway may be closed down inadvertently, and people may only go for the one big indication, because, as you know, clinical trials aren't getting cheaper, and so, the pharmaceutical companies make these business decisions, and they can lead patients in the lurch. And these are unintended consequences sometimes of when these drugs get negotiated. So, I'm extraordinarily grateful for the out-of-pocket cap and the smoothing option and stuff for these are fabulous changes.

But, like **[Participant 1]** talked about, the ability to innovate, the ability to look at combinations, the ability to look at other indications, we don't want to dampen that. That's what's kept a number of us around this table alive.

01:27:28

Moderator, RTI International

Thank you, **[Participant 4]**. Okay, well, those are all the main questions that I have for you today. I know you all have shared a number of messages already for CMS. Is there anything else that wasn't covered in our discussion today that you feel is important to share with CMS before we part ways?

01:27:48

Participant 1 (registered as a representative of a patient advocacy organization)

I'll just reiterate my offer to have you all follow up on the mantle cell through CLL Society, and also we'd like to follow up on the questions raised today about the ability to access on-label, off-label treatments and impact on commercial versus Medicare pricing. I think **[Participant 7]**'s comment is really important for the commercial market, what negotiations will affect pricing there, which will lead to additional toxicities on that side.

01:28:27

Moderator, RTI International

Thank you for reiterating, **[Participant 1]**. Any other messages that should be shared with CMS before we part ways?

01:28:36

Participant 4 (registered as a representative of a patient advocacy organization)

I would add that it's extraordinarily grateful for this opportunity. Having people with expertise in CLL, CLL is a rare cancer, and the average hematologist sees one or two new cases a year, but the centers of excellence that see a lot of this might have 20 people in their waiting room. So, I would ask that the same for CMS, when they're making these decisions, that they're consulting people who the bulk of their practice is CLL, not general hematology that they're involved. Bluntly, I make this argument more strongly with the FDA, because sometimes I'm arguing in front of people who bluntly never seen a CLL patient.

But I think CMS has that same responsibility. When you're making decisions that are going to affect the life of CLL patients, talk to a real CLL expert, somebody who's published a bunch of papers, who's been a PI on a bunch of research. Who knows CLL that's who you have to get involved in these decisions.

Closing Remarks

01:29:38

Moderator, RTI International

Right. Thanks, **[Participant 4]**. Well, thank you again to all of you for participating in today's group. We really appreciate you all taking the time to talk with us today. Your experiences and input were extremely valuable and will help inform CMS' negotiations for these drugs. CMS staff have been listening to the roundtable and will be able to bring your perspective back to their teams. **[CMS STAFF]**?

01:30:04

CMS Staff

Yeah, I just want to echo what you were saying. Thank you, guys, for sharing your thoughts. We're really grateful for it, and you've given us a lot to think about. So, thank you very much.

01:30:15

Moderator, RTI International

Thanks, **[CMS STAFF]**. Okay, if you have any questions following today's session, you can submit them to the mailbox listed here, IRARebateAndNegotiation@CMS.hhs.gov, and again, thank you all so much for sharing your perspectives today. We appreciate it.

01:30:34

Participant 7 (registered as a representative of a patient advocacy organization)

Thank you.

01:30:35

Moderator, RTI International

Have a good one, take care.

01:30:37

Participant 4 (registered as a representative of a patient advocacy organization)

Thank you.

=== END OF TRANSCRIPT ===

For a list of the drugs selected for the second cycle of the Medicare Drug Price Negotiation Program, click on the following link: https://www.cms.gov/files/document/factsheet-medicare-negotiation-selected-drug-list-ipay-2027.pdf

For more information on the Medicare Drug Price Negotiation Program, please click on the following link: https://www.cms.gov/priorities/medicare-prescription-drug-affordability/overview/medicare-drug-price-negotiation-program

Appendix

Participant 1: Registered as a representative of a patient advocacy organization

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., gifts, funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 2: Registered as a patient who has experience with the selected drug; a patient who has experience with the condition(s) treated by the selected drug

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., gifts, funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
Yes	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
No	You, your spouse, or an immediate family member is employed by or holds equity interest (stock or ownership interest) in excess of $10,000 in a company or related association with direct or indirect interest in the Negotiation Program
No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 3: Registered as a representative of a patient advocacy organization

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., gifts, funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
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No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 4: Registered as a patient who has experience with the selected drug; a patient who has experience with the condition(s) treated by the selected drug; a patient with experience with other treatment(s) similar to the selected drug for those condition(s); a representative of a patient advocacy organization

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., gifts, funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
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No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 5: Registered as a patient who has experience with the condition(s) treated by the selected drug; a patient with experience with other treatment(s) similar to the selected drug for those condition(s)

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., gifts, funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
No	Direct assistance preparing your remarks from someone who is NOT a family member, caregiver, friend, or your healthcare provider
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No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 6: Registered as a patient who has experience with the selected drug; a patient who has experience with the condition(s) treated by the selected drug; a patient with experience with other treatment(s) similar to the selected drug for those condition(s)

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., gifts, funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
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No	Any other personal or professional relationship or interaction with a company or related association with direct or indirect interest in the Negotiation Program that may be considered a financial conflict of interest

Participant 7: Registered as a representative of a patient advocacy organization

Declared Conflicts of Interest	
No	Receipt of financial payments (e.g., gifts, funding, research support, honoraria, travel, or other expenses) from a company with direct/indirect interest in the Negotiation Program, in excess of $10,000 by you, your spouse, or an immediate family member
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