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"Blood Cancers: Standards of Care, Gateways to Cancer Cures"

Proceedings from Roundtable Discussion

February 25, 2016

The New York Genome Center
New York, NY

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"Blood Cancers: Standards of Care, Gateways to Cancer Cures"

A roundtable discussion, Blood Cancers: Standards of Care, Gateways to Cancer Cures, *was held on February 25, 2016 in New York City to explore the current state and impact of blood cancer research and treatment. These proceedings are based on the discussion and interactive question and answer session conducted by a multidisciplinary panel of researchers, clinicians, and advocates and an invited audience of journalists, blood cancer patients and family members, research donors and other members of The Leukemia & Lymphoma Society community.*

Executive Summary

This is an extremely exciting time in the field of blood cancer research and treatment. In just the past year alone there has been remarkable progress in treatments for patients with multiple myeloma and chronic lymphocytic leukemia, just to name two, and emerging approaches in immunotherapy and precision medicine that are showing great promise.

Advancing blood cancer treatments and cures also means advancing the science and treatment of other types of cancers and certain chronic diseases as well. Since 2000, more than 40% of all the newly FDA approved cancer drugs were approved first for blood cancer and many are now used to treat other forms of cancer and non-malignant diseases.

At the same time, the death rate from certain blood cancers remains stubbornly high, with treatment protocols that haven't changed in decades. Clearly, there's much work still to be done in understanding the genetic underpinnings of blood cancers and finding new ways to correct or block those defects.

The Leukemia & Lymphoma Society (LLS), the leading global organization dedicated to advancing blood cancer cures and access to treatment, is on the frontlines of fighting blood cancers and helping patients to access lifesaving treatments and cures. With a firm belief that changing outcomes depends on collaboration and the sharing of ideas and knowledge, LLS convened the country's leading experts in blood cancer research and treatment, along with representatives from the biopharmaceutical industry and patient advocacy, to explore the state of blood cancers from their unique perspectives.

Laura Landro, assistant managing editor and columnist for *The Wall Street Journal*, and a chronic myeloid leukemia survivor, served as moderator of the roundtable. She engaged the panelists in a lively conversation that focused on several key areas:

- The role of collaboration among research institutions in finding new treatments for blood cancers.
- Advancements in precision medicine and the impact it will have on the development of cancer treatments.
- Venture philanthropy as a model that can drive discovery and development of new treatments.
- Ways to address cost and access to new drugs and other cancer treatments.
- The need to involve the patient's perspective when creating patient reported outcome measures.

The following are moderator and panelist remarks, as well as responses from a lively Q&A, as recorded during the roundtable. These have been lightly edited for clarity. A video of the roundtable also can be accessed at https://youtu.be/2U-I3GV0FVA.

Introduction

Laura Landro, Assistant Managing Editor and Columnist, *The Wall Street Journal*

As a survivor and as a journalist, I am fascinated by all of the research affecting blood cancers. When I was diagnosed nearly 25 years ago, it was a very different world. For CML, a bone marrow transplant was really the only curative option, and drugs like Gleevec were still a long way off. Not only that, as a patient it was virtually impossible to get information. There was no Internet as we know it today and no way to get information. It was very difficult to find medical literature. Clearly, a lot has changed. I think I'm as interested in this topic as an activist patient.

The reason I started *The Wall Street Journal* column “The Informed Patient” is because it is really important, as patients, to understand what's happening, to read the biomedical literature to the extent that it applies to your specific situation and to try to keep up with the latest research developments. I regularly plough through medical journals and the American Society of Hematology abstracts to learn about the latest findings.

Our panel represents, in a way, the blood cancer spectrum, from researchers to industry to clinicians to patients. I am going to ask each of them to tell us what they believe to be the state of blood cancers, including the most exciting things that have happened in the last year.

Chapter 1:

Progress and Promise in Fighting Blood Cancers

Louis DeGennaro, Ph.D., President and CEO,
The Leukemia & Lymphoma Society

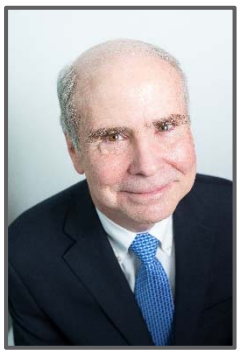
It's never a good time to get cancer but it's a phenomenal time to be fighting it. We're finally seeing the value in the investment that the country made in the Human Genome Project in the late 1990s and the early 2000s. That investment is really providing value in cancer and in the blood cancers. New technologies and new methods of finding pathways, targeting those pathways, developing new therapies, new modalities that just really didn't exist before – this is what makes it so exciting.

The pharmaceutical industry has stepped up in a tremendous way as well. There are over 900 drugs for cancer in clinical development, and nearly 300 of them for blood cancers. This is the result of the partnership between academic science driving the early discoveries and underpinnings of the causes of the disease paired with significant pharmaceutical industry output in the development of new drugs.

Patient-focused groups have had a bit of an epiphany, and they're applying for-profit industry best practices to how they operate. This includes organizational structure that leads to more efficient and effective deployment of donor dollars and ways of communicating that provide more robust connections with patients. Volunteer health agencies and patient advocate groups are recognizing for the first time the key role that they can play in bringing together the entire ecosystem around the development of new therapies for patients. Organizations like The Leukemia & Lymphoma Society can bring together academic research, the regulatory agencies, the payers, the patients, and the pharmaceutical industry in a way that can promote collaboration and yield an acceleration of new therapies.

Chapter 2:

Moving Faster From Bench to Bedside Through Collaboration



Kenneth Anderson, M.D., Program Director, Jerome Lipper Multiple Myeloma Center and LeBow Institute for Myeloma Therapeutics, Institute Physician, Dana-Farber Cancer Institute; Kraft Family Professor of Medicine, Harvard Medical School

I've worked at Dana-Farber Cancer Institute for more than 35 years on a disease called multiple myeloma, which, when I started out, was a fatal bone marrow cancer and people died in only a few months. Now it's often a chronic illness in many patients, and survival has extended at least three- to four-fold, with much more promise in the future.

So the question is, why focus on blood cancers? Just to remind everyone, the first treatment of blood cancer—for cancer in general—was in the blood cancer acute lymphoblastic leukemia (ALL). The principles of how we use conventional chemotherapy were all established in blood cancers. It's only appropriate that blood cancers, as a model system, can now lead the way towards progress much more generally in cancer.

In that regard, there are two trends that have really made a difference. What happened in multiple myeloma in the last year? Everything did. In the past 12 years we have had 16 FDA approved treatments; but in the last year, we've had seven new treatments in multiple myeloma and four new drug classes, an indoor world record in multiple myeloma.

What's the significance of that? It's obvious. Patients are going to do much, much better as a consequence, forevermore. The reason it happened is the translation of science from the bench to the bedside, an unprecedented knowledge of the mechanisms of cancer that are occurring inside of the cancer cell at the level of the genes, what we call epigenetics. Secondly, an understanding of the microenvironment; we've been able to make model systems targeting not only the cancer cell directly but also targeting the mechanisms that allow that tumor cell to live and grow and survive in the bone marrow.

Besides this precision medicine emphasis is the huge emphasis on immune therapies understanding what it is in the host that may help us to restore the ability of the patient to reject his or her cancer. Precision medicine and immunotherapies are, to me, the most exciting trends for the future.

How progress is being made is akin to a team sport. The team includes those that do academic research, both laboratory and clinical. The second members of the team are the biotech and pharmaceutical companies. The funders of research, which include LLS and National Institutes of Health and other sources, are part of the team as are the regulators, who often are not given enough credit. I must single out the FDA in terms of blood cancers because they could not have been more proactive. It's not an exaggeration to say that we would not have had this progress if the FDA had not had patients as their first priority and worked double time to allow seven approvals in one year to happen.

Finally, besides the investigators, biotech and pharma, funders of research, and regulators, the most important part of the team are the patients who are our heroes and inspirations. That is a winning team. I think if we can appreciate the progress we've made together in the past and figure out how we can make this progress count for patients, the future is even brighter than what we've seen in the recent past.

Chapter 3:

A Shared Sense of Urgency to Find New Therapies

Ross L. Levine, M.D., Member, Human Oncology and Pathogenics Program, Attending Physician, Leukemia Service, Department of Medicine and Laurence Joseph Dineen Chair in Leukemia Research, Memorial Sloan Kettering Cancer Center; Professor of Medicine, Weill Cornell Medical College

I am a leukemia clinician and researcher at Memorial Sloan Kettering. I decided to work on leukemia because when I was a fellow at Dana Farber in Dr. Anderson's department in 2002, virtually every patient I took care of who had leukemia died of their disease. And almost all of them died in the year that I took care of them as a trainee. That just didn't feel right; it didn't feel like a successful outcome for almost anybody. It created a sense in many of us who were entering our careers of urgency, of impatience – the idea that we needed to do better and we needed to do better fast.

For me, the tremendous moment occurred when I was still in training in Boston. I was involved in a collaborative effort through which we discovered mutations in a gene called JAK2 in a set of chronic leukemias and which we knew nothing about, and thus we were able to discover a new target. We worked with industry partners and academic partners and conducted clinical trials to test new drugs. A drug was approved six years later—from a discovery in 2005 to a drug in 2011. That for me, really whetted my appetite to be part of the solution for a much bigger group of patients with more difficult to treat diseases.

So the question I asked myself is, "how do things look right now? How do they look for us as a field?" I think the exciting thing for me is the idea that these individual examples—and I was so fortunate at an early point in my career to be part of that—were occasional examples. Every year or two we make a discovery and we find a drug that we tailor to subsets of patients. Going to the American Society of Hematology (ASH) meeting this year and walking around the room, there was the potential for similar discoveries in every corner of the meeting and at every lecture and every poster. It's not about finding one drug or one solution for all our patients, but that young, smart, engaging people and groups are finding new targets. They're nominating new ideas, and these opportunities are just exploding in front of us.

The challenge is, how do we then take this knowledge, which is telling us that we're not treating one leukemia but many different flavors, and how do we match that with lots of new drugs that work in many different ways? The exciting thing about ASH this year was that we're seeing success. We're seeing examples where drugs, if they're tailored to the right target and the right group of patients, can have massive improvements in outcome. More effective. Less toxic. They work in new ways.

How do we take these successes and build on them and work together? Break down the walls. Whether you're a patient or a doctor or a researcher or a regulatory expert or at a biotech or large pharmaceutical company, how do we all break down the walls? I was just really encouraged more than anything at ASH at the dialogue, the idea that everybody is in this together. There's this incredible sense that we can actually all work together. To me, the thing I go home with when I'm on the plane for a meeting like that is the sense that we're at a moment where there's discoveries and a willingness to work together to leverage those discoveries. I really believe the time is now.

Chapter 4:

The Financial Toxicity of Cancer Treatment and Care

Rena Conti, Ph.D., Assistant Professor of Health Policy at The University of Chicago, Department of Pediatrics, Section of Hematology/Oncology, and Department of Public Health Sciences

I'm an economist at The University of Chicago, and my expertise is on drug pricing and availability. I think the thing that's happened in the past year in my world is that cancer treatment availability, affordability and, frankly, toxicity has become a major issue for patients, their insurers, their employers, and their families. Spending on cancer treatment has exploded. It's high in terms of level but really it's the growth in spending that is worrisome to us all. This growth in spending is outpacing all other spending on dreaded diseases that are much more common, such as heart disease and diabetes. They also are outstripping wage growth in the United States.

The media and various politicians have been stoking the fire of outrage over cost. Much, but not all of this concern has focused on drug pricing. I think the average cost of treating a patient with leukemia is currently around $120,000 per year. It's almost as if affordability is a microcosm of the larger discontent of corporations getting rich and the little guy is paying.

Amid the media circus, there's something real here. I think the key fact is the following: the average median income in the United States is $51,000 per household. That is nine percent lower than its peak in 1999 and is at the same level as when President Reagan was in office. The recovery from the last recession has not translated into higher wages, and my colleague has just recently published a study suggesting that we are experiencing a hollowing out of the middle class.

As my mother also reminds me, for those elderly folks living on a fixed income, Social Security remains a major source if not *the* major source of income. These seniors are living on a monthly budget of approximately $1,000. What this means in practice is that patients are every day in this very uncomfortable position where they have to face trade-offs between affording their cancer treatment and dealing with all of the other expenses they have in their lives.

We are just at the beginning of understanding what financial toxicity really means, both in terms of its causes but also in terms of its consequences. I believe that only with systematic examinations of both causes and consequences can we identify potential policy solutions that families, employers, insurers—even drug companies—should be able to get behind to both make sure that patients can access these incredible miracle breakthroughs of scientific progress, but also not kill incentives to innovate and bring the next Gleevec into the world.

Chapter 5:

Pursuing Drug Development While Ensuring Patient Access

Michael Ybarra, M.D., Senior Director of Alliance Development, PhRMA

I am an emergency physician, although I want to bring the perspective of the pharmaceutical industry as well. I work on the policy and advocacy side at PhRMA, the trade association in Washington D.C.

We all experience the personal aspects of cancer and blood cancer. It's something that's affected my family as well, something that actually led my dad to pursue medicine. He is one of three children but his youngest brother passed away in 1958 from acute lymphoblastic leukemia (ALL). In 1958 the survival rate was roughly three percent for ALL, and in 2010 now we're living in an age where it's 92% survival rate. That was something that clearly impacted his decision to go into medicine and led to a whole family of doctors, including myself, all pursuing different specialties but really understanding that patients do have unmet needs.

I can say that in my work at PhRMA with public policy professionals working with our member companies, we all have that goal. We all go to work every day because we want to sustain a policy environment that allows for innovative therapies. That doesn't mean we don't recognize everything that's being talked about in the news.

About a year ago we worked with The Leukemia & Lymphoma Society on a quarterly medicines and development report. That report focused on blood cancers. It found that there are nearly 300 medicines in development, with about 250 medicines in development in the pharmaceutical pipeline to treat blood cancers. If you want to look at just the science, it's monoclonal antibodies that target PD1 in order to treat Hodgkin's lymphoma, new treatments for hairy cell leukemia, antibodies for multiple myeloma, tyrosine kinase inhibitors for AML. There's incredible science going on.

The value is clearly there. I think the ALL example is the perfect one. We were three percent in 1964. We're at 90% now. That doesn't mean that there is not unmet need, and that doesn't mean that there are not issues. As it pertains to cost, we focus on the access and affordability issues. The things that we go to work for are to make sure that patients can afford to not leave their medicine at the pharmacy counter. It doesn't benefit any of us when a patient doesn't leave with it.

I still see patients on a weekly basis and it's something that I deal with and have to talk to my patients about. We have to follow up and make sure that we picked the right medicine for their insurance plan, that the co-payments are affordable to them; and if they are not affordable, we have to troubleshoot and work through that. That's one of the very challenging parts of being a physician. I can only imagine it's even harder if you're a specialist in hematology/oncology because my prescribing patterns are much different for a different set of medical problems.

We realize that financial burden is there and a lot of that is augmented by the changes that have occurred in the last five years with the Affordable Care Act. Five years ago most patients in this country did not have a deductible; most patients paid a fixed co-payment for their prescription medicines. So now we're at a time where our companies have brought to market incredible therapies

that are intended for a very small patient population, on the grand scale of drugs of the 1990s which were intended for a large number of patients in the country. Many people at some point are going to be on a statin, for example.

These new medicines are incredibly targeted. They take incredible science to bring them to market. They're for a small patient population. That–coupled with the fact that now patients are faced with very high out of pocket costs because their plans are designed in such a way that they have to meet a certain deductible--they have to get to that deductible, and so they go to the pharmacy counter and they have to pay hundreds of dollars out of pocket. If you're on a fixed income, that is clearly a challenge. We recognize the financial burdens and we advocate for things that will hopefully make medicines more affordable for patients so they will be able to have the medicine that can hopefully bring a cure.

Just to put the overall cost in context, in 2014 spending on cancer medicine was roughly one percent of all healthcare spending. For an extremely, obviously very sick population, this is high stakes medicine. This is incredibly important. In terms of solutions, we want to be a part of the solution. We think innovation is part of the solution. Targeted therapies that work for patients are a good investment. If we know the therapy is going to work for that specific patient, that is a good investment. We really believe in the competitive market and we want to make sure that patients benefit from the competitive market, and are able to benefit from the negotiations that our companies have with pharmacy benefit managers.

Generic and brand competition help keep spending in check. We think that insurance should be adequate and should be affordable, and we want to make sure that patients are not subject to excessive cost sharing. We've all experienced that. I personally have experienced that when medical claims, hospitalization, are more expensive than prescription medicines. We've all been there.

Our member companies have stepped up to the plate in terms of patient assistance programs. Partnership for Prescription Assistance (PAP) is PhRMA's overarching patient assistance program. We've helped almost 10 million people access their medicines just through PAP alone.

Chapter 6:

The Collateral Damage of Cancer Treatment

Susan Love, M.D., M.B.A., Chief Visionary Officer,
Dr. Susan Love Research Foundation

I have a unique perspective because I spent most of my career as a breast cancer surgeon. I started out at Dana Farber. I was at UCLA. I've done research. I'm an author and an advocate and a general rabble-rouser. Then all of a sudden about three and a half years ago, I was diagnosed with acute myeloid leukemia (AML). I was feeling perfectly fine. I had a routine blood test and got called back. “Come right back to the hospital. You have 30% blasts in your blood.” I'm a breast cancer surgeon. I couldn't even remember what blasts were. I'm driving back to the doctor’s office asking myself, “What does that mean?”

I ended up being hospitalized and I had chemotherapy, which failed me. We often say you failed chemotherapy. I say, “No, chemotherapy failed me.” We sometimes lose track of that. I ended up with a bone marrow transplant from my younger sister, who is 12 years younger, so I figure that gives me a new lease in life.

It was a very humbling and eye-opening experience. I was really amazed at what a crude way to treat a disease that really hasn't changed since I was in training in medical school when I graduated in 1974. It's really treated about the same way as it was then, which is high dose chemotherapy and then try to recover by giving you a transplant. It's like the radical mastectomy. We've gone a lot further in breast cancer in terms of figuring out targeted therapies in different kinds of breast cancer but in some ways you could argue that the bone marrow transplant is the original immunotherapy because of the graft versus leukemia effect. In some ways it's really archaic, and in some ways it's novel and moving forward.

The really big surprise to me of the whole experience was what I call the collateral damage. When you're a doctor looking at a patient with cancer you compare them to the people who died, and you're patting yourself on the back for having done such a great job. When you're the patient, you're comparing yourself to how you were before. You're acutely aware of the price you've paid to be here. You're happy to be here but you're very aware of the peripheral neuropathy and the chemo-brain and all the other consequences, which we euphemistically call side effects. But they're not side effects. Side effects are temporary. That's like throwing up when you get chemo. These are permanent. It's more like you're in a car crash and you get your car fixed but that passenger door never opens the same away again as it did when it was new. That's how your body is afterwards.

As we're making more progress in treating these cancers, we have to start paying much more attention to the collateral damage. Not just acknowledging it but also doing research on it because maybe the same precision medicine that's allowing us to direct some of our treatments more precisely may be able to tell us who’s more susceptible to a certain side effect or consequence. We never really look at that. We should be starting to look at whether people who have dementia in their family get more chemo-brain. Maybe if you have restless legs you get more peripheral neuropathy because you have some kind of nerve issue. Maybe there's a genetic marker that could predict that.

Both in the breast cancer world and now as an advocate in the LLS world, there's a movement to do patient reported outcomes. My complaint about this is that the patient reported outcomes are coming from questionnaires developed by doctors or researchers for patients to fill out. There are only the questions that the doctors know about or are interested in and they miss the things that actually are happening to the patient.

We've got to start asking patients directly so they can really be patient reported outcomes. What are the things that are bothering them and interfering with their lives? We're trying to do this with my non-profit foundation on breast cancer but it's something that I would advise everybody in pharma and research to be thinking about as well. Otherwise we're going to save all these lives and our statistics will look great but the patients will be feeling terrible and not that functional. That's not what we want.

Chapter 7:

The Patient Perspective: Life After Successful Treatment

Erin Zammett Ruddy, Author, Blogger, Survivor

I am a patient survivor. I was diagnosed 14 years ago when I was 23 with chronic myelogenous leukemia (CML). I didn't have any symptoms. I went in and had a blood test, and they called me back. A bone marrow biopsy confirmed that I had CML.

Hearing you have cancer at 23 is obviously devastating, but this was November of 2001, which was six months after Gleevec was approved by the FDA. It actually was a really good time to be fighting CML because I was able to get right on the drug. I went to Oregon Health and Sciences University and met Brian Druker and his colleague, Michael Mauro. They were running trials at the time to see if they could make Gleevec more efficient, so I wound up doing a trial combination of Gleevec and Ara-C injections that I gave myself. I was terrible at it and I hated it but it was a small price to pay. I wound up doing really well.

Gleevec was being touted as a miracle drug, and for me it was a miracle. Within a little over a year of my diagnosis I was in complete molecular remission. I was living a normal life. I really didn't have major side effects at all but literally on the same day that Dr. Mauro called me to say that I was in remission, my sister called and told me that she had been diagnosed with Hodgkin's lymphoma. She was 27 at the time and seven months pregnant.

We were back to square one and there is no magic pill for Hodgkin's lymphoma. So she went through the grueling treatment, chemo and radiation while she was pregnant and then after. She relapsed after ten months and went into Memorial Sloan Kettering and spent a month there having a bone marrow transplant. It was a crazy time for all of us, for our family, but she did incredibly well. The little boy that she was pregnant with is now a whip-smart seventh grader and the star of his baseball team. She was able to have two more kids post-transplant and they're all fantastic. She's doing great.

As for me, I have three children and I was able to stop Gleevec three different times to have them. I was one of the first people to do this so I do communicate a lot now with people who want to go off the drug and have babies. I worked very closely with Dr. Druker and Dr. Mauro. We thought about it and made the decision to do it. I went off for about ten months each time and my cancer never came back. Those little mini experiments, as we refer to them, are what led me to make the decision a few months ago to join a discontinuation trial that they're running at Memorial Sloan Kettering.

Michael Mauro has since moved from OHSU to Memorial Sloan Kettering, which worked out well for me, so I didn't have to go to Oregon anymore to see him.

In November, 14 years almost to the day that I was diagnosed, I took my last dose of Gleevec and what I hope will be my last dose of Gleevec. I'm a writer and I wrote an article where I talked about grappling with the decision. Gleevec was so good to me. I owe my life to Gleevec. I know how lucky I am to have had a pill to treat my cancer. I didn't have to go through what so many other people have gone through, what my sister went through. So I really grappled with it. I felt like I was looking a gift

horse in the mouth. I didn't have too many side effects to speak of. In the article, I said it was like breaking up with a great guy. “Hey Gleevec, it's not you, it's me.”

I was at Memorial Sloan Kettering yesterday and I had my third blood test, so it's month three since I've been off. The name of the study is the LAST study, Life After Stopping TKIs. It's exciting to be a part of this trial. I feel like I was part of the original Gleevec story 14 years ago and now to be part of what could be the next chapter, I'm excited. I felt I owed it to myself to see what life is like off of medication and to the cancer community to see if this could be the next step.

I will say that the past 14 years have been very lucky for my sister and me. We know that there are a lot of people who aren't as lucky, which is why I have devoted my life to LLS and to being around people who are doing the same thing. It's an honor.

Chapter 8:

Advancements in CLL

John Byrd, M.D., D. Warren Brown Chair of Leukemia Research; Professor of Medicine and Medicinal Chemistry and Director, Division of Hematology, Department of Internal Medicine, The Ohio State University Wexner Medical Center

I'm a hematologist and a physician scientist that does most of his science in the clinic and in the bedside. My area of research is chronic lymphocytic leukemia, and I'm drifting back now to acute myeloid leukemia.

I'll introduce CLL and then go to what I think are the most exciting things that have happened this year and the promises to come. CLL is the most common adult leukemia in terms of prevalence and there's not a curative therapy for this. For decades, there was not an effective therapy—we had chemotherapy, but it palliated the disease. It didn't prolong survival.

At about the same time Gleevec was coming into the clinic for CML, there was the first targeted drug tested in CLL called rituximab. We were blessed to be part of the team that introduced that in CLL and combined it with chemotherapy. We want to get rid of chemotherapy in CLL. We want to prolong survival in a meaningful way. A significant thing that came forth this year were three publications published in the journal *Blood* that showed that when you add rituximab, a targeted therapy, to chemotherapy in a subset of CLL patients you can potentially cure their disease. A 14 year follow up showed no CLL after receiving this combination, so that's a striking finding.

Unfortunately, I hear what Dr. Love said about the after effects because when you look at the long-term follow up of this treatment in the patients that were cured of their CLL, they were left with a high frequency of secondary cancers that ultimately compromised their potential to get on with life and stop worrying about another cancer. That really emphasizes the importance of moving forward with other approaches.

The second group of targeted therapies for CLL was Bruton's tyrosine kinase or BTK. The first trials with ibrutinib started in 2009, which we didn't think was going to work because, unlike CML, CLL doesn't have a single target. Everyone said it was unlikely that one precise medicine was going to work. I heard that from 1997 when I started as an attending physician.

In fact, ibrutinib threw away that doubt. It started in trials in 2009. We saw dramatic responses in very refractory CLL patients taking a pill once a day and often coming from hospice. I am here as the person that's treated 300 or more patients with this drug and have heard patients say this drug not only gave them their lives back but it made them feel the way they did before CLL. For some of the patients that were in the early trials, it also set them up to have more money while they were living with CLL because they saw the drug was effective and they bought stock in the company.

That brings us to now. Where do we get to with ibrutinib in 2015 and beyond? There was a very exciting study presented at the annual ASH meeting describing the RESONATE-2 study, which looked at ibrutinib as a first-line therapy versus chlorambucil, which is the first chemotherapy used in CLL. It's not very good, but they looked at this in elderly patients. Of course, ibrutinib beat the socks

off of chemotherapy. Very favorable side effects. Very favorable outcome. Improved survival. All the endpoints that doctors look at.

What I found most inspiring about that study is an analysis that's very similar to analyses that I've seen with CML. Patients can go on a pill, and they have to stay on a pill. We're not quite wrestling with the question of stopping ibrutinib yet, but we're already talking about doing it in patients that have done real well. They can live potentially as long as they would without CLL. That same story has been true with Gleevec, and so that was a very inspiring finding.

The long-term follow-up is not showing a lot of the “chemo-brain” side effects and other bad side effects. In fact, it's showing that these targeted drugs may make the immune system work better. Why is that exciting? Because we've heard a lot of excitement about immune therapies, the checkpoint inhibitors, the CAR T-cells. In fact, these drugs make the CAR T-cells, which could have the potential to cure CLL, work even better. CLL has taught us that targeted therapies can work across a disease if you have a good drug and you have a target that spares normal tissue. Looking forward in this disease, we're seeing the same second generation medicines that may take away some of the side effects of ibrutinib. We heard about acalabrutinib and other targeted drugs where we might be able to give two or three targeted or immune therapies together to put patients in complete remission and cure them of the disease without chemotherapy’s long-term adverse events.

Chapter 9:

Questions and Answers

Laura Landro: It's very encouraging to hear about all the collaboration that's going on, to know that there are big groups working on AML. We all know that there's another big blood cancer collaborative going on in the country, another moonshot. Also, to hear how the FDA has been so cooperative.

I actually just reviewed a book by Dr. Vince DeVita, which is in many ways the opposite of everything that's been said. No one collaborates. It's all institutions trying to get their own papers published and get their own drugs out there and that the FDA process for doing this is totally flawed and needs to be completely overhauled. I'm curious with some of the folks that are dealing with this at the comprehensive cancer centers. Is that wrong? Is that changing? Is that the way it was and is it better now, particularly in the blood cancers?

Dr. Byrd: Having seen the FDA at work with ibrutinib, which was so impactful to patients, every day that drug wasn't approved patients were going to die. So the FDA worked hand-in-hand with the pharmaceutical companies. I've been warned not to say this because they're in the government and they could get in trouble. They worked when they weren't supposed to be working to make this drug available and to communicate. There are some barriers that they have because they have to work within the law. Changing the law of how drugs get approved is going to help them work, but they get the blame and they're really trying to approve good drugs. We heard that as well for acute leukemia.

Dr. Anderson: I also want to cheer for the FDA. What's happened at the level of the FDA—and it has changed—is a recognition of a whole new field called regulatory science, so that those who work at the FDA are every bit as motivated to make progress for patients. What this regulatory science field means is that they learn about the diseases. They learn about what would be a good clinical trial to show, on the one hand, efficacy and, on the other hand, lack of side effects.

Once a drug looks promising, they work double time to make sure that this gets a very rapid review. We have new breakthrough status at the FDA. Part of the excitement is now that we have these new targeted agents in all of the blood cancers, the endpoints that were relevant even the last year or two in terms of how long people live without active cancer are not so useful anymore to try to develop a new medicine. People are living many, many years. That's a wonderful outcome. If you have a new medicine and you want to get it approved in blood cancer and you're working in tech, biotech or pharma, we can't wait.

Most importantly, the patients can't wait. With blood cancers, our goal in clinical trials is to identify new biomarkers so we can better predict whether a patient is going to survive 10 or 15 years and then connect those patients with the most effective therapies. The FDA could not be more passionately and personally committed to patients with blood cancers.

Ms. Landro: Well, that's interesting to hear. As I said, it seems to me everything gets approved in Europe first.

Dr. Ybarra: I just want to add the industry perspective here, which is in agreement. I tend to be a glass half-full person. We are working collaboratively but there are always ways that we could break down more barriers. Industry does play a key role in trying to build bridges with academia. The funding piece is really critical. The biopharmaceutical industry's contribution to the funding of

research is really important. Grant writing and grant requests are clearly important from the NIH, but the industry is about $51 billion per year in R&D spending. That's really critical.

In terms of ways that we could improve the process, just breaking down barriers and improving the clinical trials, we are active in the regulatory process for developing and validating biomarkers. A clear and transparent regulatory framework and incorporation of more diverse data sets could be helpful.

Dr. Levine: I just want to pick up on the other question you asked, which was the issue of silos that Laura mentioned in reference to Dr. DeVita, who has had as big an impact on patients with lymphoma as probably anybody in the history of the disease; we should not forget his impact on the development of modern chemotherapy for Hodgkin's disease.

The reality is that we all recognize that in academia, any industry, and any job, there's an aspect of feeling the need for individual accomplishment. That is part of what makes this country great. None of us wants to ever discourage people from wanting to do the best they can. The mantra that I believe more and more and what I see happening over and over again is the idea that if what we do has impact—if we do it together, there's more than enough credit and success to go around. What I see are more and more examples of all kinds of flavors, different academic institutions that didn't work together before, different companies working together, examples of public and private partnerships. This idea that when success becomes likely it creates a culture where the end result for everybody's individual careers and for our patients is much, much greater than if we went out by ourselves.

I think that, combined with the idea of big data, we need to not just look at our 20 patients in our center that have AML in the past six months but develop data sets and ask what happens not just at Memorial Sloan Kettering or Dana-Farber or Ohio State, but what happens in a private practice around the corner from Memorial Sloan Kettering that treats as many AML patients as we do. By combining our forces to understand what we learn from every patient we treat, we're going to learn a lot more.

It's going to take time. It's something that many of us really believe in, that LLS has been pushing us to do. I really believe that that's a cultural change that's already occurring and has to continue to occur. It's something that we have to continue to talk about very openly because it's something that we have to push ourselves, all of us, to continue to do better.

Dr. Love: I think that's true, but I think one of the things we're going to have to do too is make the rewards be rewards to teams and not individuals. When the prizes are all to individuals—as are tenure and promotions—all the rewards are still individual-based. If we're really going to be able to incorporate that teamwork, we're going to have to change the reward system.

Ms. Landro: This gets into the idea of venture philanthropy. There are a lot of interesting things going on in that field, but people are certainly skeptical about it. You see things in other diseases like the Alzheimer's Drug Discovery Foundation. That is the original “we're just going to give money to people who are working on the discovery of drugs.” Is that a model that fits into your thinking about the future of blood cancers discovery?

Dr. Anderson: I absolutely think so. Part of this issue about who gets credit, is honestly, to me, a real discussion, but it's kind of an empty discussion until someday these diseases are cured. Then we can actually give credit, especially to the patients who enrolled in the trials. To be honest, the system right now for developing a new medicine from the bench to the bedside really needs improvement. The idea that Dr. Levine or Dr. Byrd and I or others in biotech and pharma are trying

to do new science and find a new target is absolutely real. The entrepreneurial spirit in that regard is a good thing. Much of it is going on in the U.S. When you find a new target and it's validated in preclinical systems, our system is that it then goes from the bench to the bedside. Honestly, until recently the idea would be we would find a target and then we would look around the world and hope that there was a biotech or big pharmaceutical that had a drug already or would put in the commitment to try to help make it.

That still goes on, and I don't want to at all downplay the role of biotech and pharma because it's essential in order to take this scientific advance and, as I like to say, make it count for patients in terms of improving diagnosis, prognosis, or treatment. I want to sing the praises of Dr. Louis DeGennaro and The Leukemia & Lymphoma Society. In this model of venture philanthropy, the idea is that now when a new finding comes along and Dr. Levine or I or Dr. Byrd finds something novel that we can move closer to the bedside than ever before; it can happen through a program called the Therapy Acceleration Program.

Through this venture philanthropy prototype, medicines can be made. We're involved in a very wonderful, successful effort now with LLS that, when that medicine becomes successful, will put funds back into LLS. This will be a machine that will keep making sure that the new good ideas that are rigorously validated actually get to patients. We're doing similar efforts now with a vaccine that also looks quite awesome. Just as you've heard about in terms of the wonderful science around precision medicine and immunotherapies, we do not need to be thinking about credit; that's the last thing we need to be thinking about. We need to be thinking about how we can make sure at this unprecedented time in science that we keep the promise that we made to patients, that we take the best science and make sure we get advances to them at the bedside most quickly. That is a very innovative program that LLS is leading. I want to really thank them for that effort.

Dr. DeGennaro: I mentioned there had been an epiphany in the not-for-profit world. I think this is part of it. Charities that are involved in funding research in diseases have recognized that in order to really succeed in their mission, the mission being new therapies for patients, cures for patients, they need to be involved across the entire spectrum of the process of actually getting those drugs to patients. It's not just supporting academic research. There's a vital component that the industry is involved in, and that's part of it.

It's also interplay with the Food and Drug Administration. The reality is, as a not-for-profit, we have an entrée to the FDA to provide them with unbiased information and education in a way that many folks don't. That's an important part of our role; likewise, with regulators and, of course, with patients as well. When you begin to think about the entire ecosystem of bringing a therapy, potentially a cure, to patients there's a true role for organizations like LLS in doing that. Venture philanthropy is certainly a part of it, and we're proud to be a leader in that arena. We're proud to be a leader around that entire ecosystem.

I can't help but be struck by the tremendous advances in science that we're discussing. There's great opportunity in the future. Yet we heard a lot about access issues. I think it's important to note that if patients don't have access to these lifesaving therapies none of us in the room have done our jobs.

Ms. Landro: I was talking with Ms. Ruddy earlier about the costs of these drugs. When I had a bone marrow transplant it cost a quarter of a million dollars in 1992. I don't know what it's up to now, and later, when I had to take Gleevec for a relapse, it was a $30 co-pay. I think Ms. Ruddy, you said that yours was $50. As a patient with insurance you don't think about these things as much, but, as

you've said, Dr. Conti, that's very much a problem for many people. We're privileged to have been able to have these therapies without those concerns.

What is the solution? There are ways people can get help, but is it enough and what model can you take to do all this great biomedical research, invest all this money, and then get access. What are the things that we can do for this?

Dr. Conti: The price of bone marrow transplant actually hasn't changed, which is good news. But I think there are a couple of issues. The first is that although there's a lot of focus on the cost of the drugs, that is not the only component of cost that patients are feeling. Specifically, we just published a study suggesting that it's also the site of care that really determines how much patients are actually facing in terms of out of pocket costs, because academic medical centers and other consolidated institutions frankly, charge higher prices. Those prices trickle down to what patients actually have to pay out of pocket.

We know that this is an issue, but we actually don't know how big of an issue it is. While we've heard a lot of stories about access being an issue, there has been no national systematic examination of exactly how many patients and what proportion of patients facing specific diagnoses are actually having trouble with paying for their drugs or paying for their treatment more generally. Exactly what types of treatments are they being offered financial assistance for, and what types of treatments they are not being offered financial assistance for?

We also don't know what the consequences are for patients facing this type of toxicity. For example, we don't know whether for specific patients they are selling their house or their car or borrowing money or taking money out of their kids' education fund to afford this therapy. We need to know that so we can actually think about solutions.

Then, finally, we don't really know how patients trade off these things. It is entirely possible that patients in their last months of life are very willing to spend all of the rest of the money they have for a cure or for even a handful of months to be with their children and grandchildren. My colleagues and I are partnering with LLS to examine what the contours of financial toxicity are. We're very excited about that. Our guiding principle is the following: there are really no bad actors in the system. There are just a lot of different actors who make a lot of money off the healthcare system as it exists now. That includes physicians, hospitals, pharma, insurers and others.

All of these institutions are acting on the current incentives that they face. If we change the incentives and make patient affordability the central focus or a central value I think we will be able to find some attainable solutions that will actually move this ball forward.

Dr. Love: I want to add that it's not just drug costs, as Dr. Conti pointed out, but it's also getting the test, the follow-up test, the x-rays, the scans, the whatever. All of those add up. Sometimes we focus just on the cost of drugs, but the MRI that you're getting for follow up or the PET scan or whatever is also just as expensive.

Dr. Conti: Absolutely, and the nature of work is changing. There are a lot of people who are consultants or who are day laborers now, so missing that day of work to take your mother to the hospital for the *nth* test that they need—

Dr. Love: Which they may really not need, but it's just our habit to do.

Dr. Conti: Those are real costs, and those costs need to be figured in and really understood so we can actually think about where the rubber is meeting the road in terms of affordability. Maybe it's not the treatment itself but it's all the care surrounding the treatment.

Ms. Landro: Obviously, this is universal for all cancers. I'd like to steer it back just to the blood cancers for a moment. I was thinking often—and I'm sure that as leukemia survivors you get these calls as well—somebody calls me and says my friend has been diagnosed with leukemia. I'll ask, what kind? Because it's either okay you're going to be fine or it's going to be really a tough road. I guess the question is why has the prognosis for some been so much better? In CLL I know for many years people didn't even treat it sometimes. It would just be a long smoldering disease that went on. In CML you went from bone marrow transplants to Gleevec and other drugs like it. In AML there are treatments, but often they fail. What are we missing here in getting better treatments? Why is there not the revolution in AML that there has been in multiple myeloma or CML? I think most people don't understand that the blood cancers are so many different ones, and some are kind of refractory to treatment.

Dr. Levine: The way I see the challenge in AML is that it's a very unique disease and opportunity because if you look at it from the lens of a scientist, if you look at it from the lens of a doctor, if you look at it from the lens of a patient, we know that it's not one disease. We know that it's probably between 10 and 20 distinct diseases that we lump together using very crude tools and we call it AML. That is important because even a disease like breast cancer where we recognize there's heterogeneity, it's probably, if you believe the scientists, four or five distinct subgroups. AML, which is rarer and more complex and where there's more urgency to treat, is 20 subtypes.

How do we recognize those 20 subtypes accurately and quickly so that we can actually tell a patient within days of treatment that “you don't just have AML; you have this kind of AML, and this kind of AML needs this kind of treatment.” The challenge in front of us is how do we put the rubber to the road? Right now in the clinic, we've been using the same drugs for more than four decades. We're using them in all 20 subtypes. We all know, whether we know all of the different nuances of the genomes, that that makes no sense. I thought it was really exciting at ASH that we're seeing examples in big and small trials of tailoring treatments to different subtypes. That's the era we're entering.

In AML, I really believe the good news is that between the 20 subgroups, the different players, the different genes, the different pathways, we actually know a tremendous amount. I'm not saying we don't need to do more sequencing, but we actually can take an amalgam. There's a lot of data out there. I think we're actually at a great moment in AML where we need to just break down the walls and begin. We need to stop thinking of it as one disease and start building the infrastructure to identify the subgroups in real practice and match them up with drugs. If we don't start doing it, we're not doing a service for anybody. To me, that's the challenge in front of us. AML is the perfect disease test for the precision medicine concept.

Dr. Byrd: I would agree with what Dr. Levine said and just want to add that you can understand the biology and that there are 20 subtypes, but if you still have the therapies that are very similar to what were used 40 years ago, you're not going to make a lot of progress. I think the exciting thing right now is that we're at a point where for all of those different subtypes of AML we have drugs that can rationally be directed toward a hypothesis. In this group, is this drug going to work, produce a meaningful benefit, and have a quick answer doing a study in 10 or 15 patients initially versus 300? Moving on, if a drug doesn't initially work but can subsequently generate impressive data, we will hopefully be able to go to the FDA and say, “Yes, we have a winner.”

Taking this approach really embodies thinking about developing drugs differently. One has to almost throw out the concept of a Phase III study, where you treat hundreds and hundreds of patients and randomize to a drug that you already know works well to something you don't know if it works well, because it's going to take a lot of time. A lot of patients are going to die with the disease while you're completing that study with a very effective drug. I think we're at a point in precision medicine where we can do that. AML is the best disease to do it in.

Dr. Levine: The other corollary or net effect if we begin to embrace that approach is the cost of doing the trials to get a drug approved can potentially be reduced dramatically. We always talk about the need to recover the investment that we make in developing drugs when we talk about the price of drugs. This idea that one thing we need to do is talk frankly about how can we reduce the cost of getting a drug approved because the corollary of that should be—and I believe is—that then the cost of using that drug after approval should decrease. If we all talk about that as being a goal and not just a net effect of unexpected benefit, then we raise the dialogue and bring this issue up earlier in the process and not just after the drug is approved.

Dr. Conti: I'm a naysayer on that argument. Fundamentally, the costs of R&D have nothing to do with the prices that are set for drugs. They're not connected. We know that the costs of or the prices of drugs are not connected to how much it costs to make that additional vial or that additional pill, but all the costs of development. They might as well not exist when a pharmaceutical company is actually pricing the drug. Pharmaceutical companies have every incentive to profit maximize. What I mean by that is that they price based on the willingness of payers to pay for these therapies. If we change the willingness to pay for these therapies, prices will come down, but if we change the cost of R&D I don't expect that prices will go down.

Dr. Anderson: The real cost that we're talking about is for patients. The cost is whatever number you want to call it, but its seven to ten or some outrageous number of years to take what looks like a promising lead and get it to approval to patients. That's the cost we're talking about. I think that's really the promise of precision medicine. To do a selected trial of an agent that's highly likely to work in a small number of patients and save not only financial costs, but saving months and years for patients.

I will remind everyone that Gleevec was probably one of the first examples of precision medicine. The approval came on a Phase I trial. There was no need to do a Phase II and Phase III trial.

Ms. Landro: By the way, that was very much driven by extreme patient activism.

Dr. Anderson: I think it's a critical part of the process.

Ms. Landro: We wrote all about it in *The Wall Street Journal*.

Dr. Anderson: That is more important today than ever. The other thing in precision medicine—and you read about the moonshot on precision medicine—it's actually the right medicine for the right patient at the right time, but it's not as simple as let's just give one medicine to this patient at this time. It includes the immune therapies. It includes combinations—so not only one medicine but a second medicine given in combination to prevent the escape route that the cancer is going to try to use to resist the first medication. I think what we're getting at is precision medicine is going to allow for the pooling of data for rare diseases, which is necessary if we're going to define the subsets in already rare orphan diseases. With a community of data we will be able to deliver on the promise, whether it be a combination of targeted medicines or an immune therapy, to deliver on the promise of taking the science and making it count for patients.

Ms. Landro: One of the things that we haven't talked about is the idea of when therapies no longer work—patients have become resistant or the medication has failed you. People do become resistant to Gleevec, and then of course there were other drugs that were lined up right behind that. I know at the Fred Hutchinson Cancer Center where I had my transplant, they often see patients for whom Gleevec and other drugs stopped working. Then they come back for transplants.

I'm sort of curious about the idea of bone marrow transplants. They aren't talked about as much as many of the drugs. We know that they're still out there. It's a pretty rough thing to go through, though I know they're working on mini transplants and less toxic ways to use the immune system. Is that still a promising area? Are you still thinking about transplantation as a key component of these blood cancers?

Dr. Byrd: Transplantation for AML is probably the best therapy we have right now. The problem is—and we just looked at 1,600 patients, a data set carried from the late 1990s to now—only about 15 to 20% of patients are getting to transplant. There are a variety of reasons for that. The therapy we give before breaks them down to a point where you can't get them into shape for transplant. There's insurance. There's donors. But what's exciting is that we're at a point where there's really no patient that you shouldn't be able to find a donor for, especially if they have a brother, sister or child.

Ms. Landro: That has amazingly evolved, yes.

Dr. Byrd: The biggest promise I see for this is it allows you to say, as soon as the patient comes in the door, we're going to take that patient to transplant. This is going to be your donor, and you're going to be able to get more patients to transplant. I looked at targeted agents as well, they offer great opportunity to integrate with this because if you can give somebody a pill that puts their disease in remission and doesn't make them have to stay in the hospital for 28 days, that's a lot cheaper, they're in good shape going into the transplant, and they're going to do better. There's still a lot of work being done in transplant and other types of cellular therapies that have come from that.

Dr. Levine: Stem cell transplantation is part of an emerging area that's building on the success of transplantation by using immune cells to treat blood cancers – this can be a bone marrow transplant using stem cells or a patient's own T-cells or even antibodies that recruit T-cells; there are a variety of modifications of the transplant regimen. The idea that the immune system is exquisitely active and able to kill blood cancer cells and in many cases cure patients is really a modality we want to use and improve and optimize and make a part of an integrated approach. One of the exciting things about it is the idea that it gives the potential for cure. We want to get patients to these exciting new immune modalities earlier on in therapy because, whenever we can, we want people to get therapies and then be done, as you heard about earlier about stopping Gleevec. We don't want, when possible, to have patients maintained on drugs if they don't need them, with the caveats that there may be long term effects even if they're off therapy. I think one of the exciting things about transplant is the idea that we have patients that get these therapies and then a year or two years later are off therapy and doing really well. It is something that we hadn't seen and I think it is really an exciting time. Now the question is, how do we extend the paradigm, more diseases, earlier on in therapies, access, and how do we do this not just at rarified cancer centers but in a broad spectrum of patients everywhere, not just in the U.S. but worldwide?

Dr. Byrd: We were talking about venture philanthropy, and the cellular therapy that Dr. Levine is talking about, the CAR-T cells, is something that nobody thought would work. So it is not the pharma companies that kept this alive so it could blossom into a therapy that works across all cancers, its LLS supporting Carl June's initial work with the CAR-T cells at The University of Pennsylvania. So it

gets back to part of what we're talking about here: the importance of LLS in supporting these early therapies that expand to a lot of other types of cancers.

Dr. Anderson: The transplant therapy idea is so exciting. Getting a stem cell transplant from a brother or a sister or an unrelated donor works because you get the person's new immune system that rejects the cancer; in ALL and other settings this has led to cure. It's just we haven't been able to do it from inside the patient, him or herself, before.

This is a case where we are learning from our colleagues in solid tumors about the concept of the checkpoint inhibitor. The idea is that the immune system is under this elegant system of regulatory control and there's a camouflage PDL1 on the tumor that interacts with something called PD1 on the immune effector cell that is programmed to kill that tumor, and it is a brake when those two molecules interact. If you take the brake off with checkpoint inhibitors in melanoma and lung cancer, and other solid tumors – wonderful results have been achieved. It is happening now in blood cancers too.

The reason I mention it is the team combination approach. We have immunomodulatory drugs, especially in myeloma, that work by turning on the patient's immune system. We have antibodies, as Dr. Levine mentioned, that target the tumor cells and then they recruit the patient's own immune system to selectively reject them. We have checkpoint inhibitors that take the brakes off the immune system. We have vaccines and we have cellular therapies. But the exciting thing is when you use them in combinations. And we're doing this with LLS with a vaccine in combination; in early data it looks like you can get a memory immune response in the patients themselves against their own cancers.

Just to make sure everybody appreciates the significance of that, if you get vaccinated for tetanus or smallpox or whatever else, the reason you never get that disease if you're exposed is your immune system remembers and rejects it. What if we could do that in a patient against his own cancer? Why is it so good? It's potent, it's selective and it's adaptable. All of our blood cancers keep changing, that's how they resist treatment; no matter what, they're continually evolving. The genetic component is very complicated to start with and it gets worse over time, and the disease recurs. But the immune system is honestly very potent and adaptable, so it can adapt. You get a cold today, you get better. You get an earache next week, you get better. Maybe, just maybe, the immune system can outsmart blood cancers.

Ms. Landro: As a patient, I always had the advantage of being a journalist and being able to get information and having friends who were scientists. Ms. Ruddy, I think you were probably pretty sharp about all the information you had to get. We have that natural instinct to dig, and we have connections. I'm curious on your thoughts about this as someone who has been your own advocate, you've advocated for others, you've written about this. What can scientists do to make it easier for patients to advocate for themselves, to keep up with all these things and to know what they should be asking about? I'm not sure that most cancer patients ever hear of some of these things or that there are clinical trials available. What would you advocate for in that case?

Ms. Zammett Ruddy: When I was diagnosed, it was November. I was working at *Glamour Magazine* at the time. The December issue had a story in it with an image of two hands with a pile of orange pills. The headline was "These Women Knew They Were Dying; Then a New Drug Saved Their Lives." The magazine I was working at had just run a story about Brian Druker and the original Gleevec trials. I just got the chills. It was so crazy. I came back and *Glamour Magazine* helped me. I got on a plane the next day to Oregon. So yes, I was very lucky. I still hear from people all the time that were diagnosed and they reach out to me a lot through social media.

But I think that what still is so crazy to me is that people go to the doctor that treated their mother's breast cancer to treat them for CML. I say “No. Go to a specialist for your kind of cancer!” There are so many great advocacy groups on Facebook and social media, and that's a great place for them. I know a lot of doctors now do get out there and talk about these things. I'm in a treatment-free remission group. It has people from all over the world and there is some really interesting sharing going on. I think that's what's so great and I always tell people to do that. It sounds like you're not going to get the best information on the Internet. That's always the first thing you tell people, “Don't go on the Internet. Don't Google your disease when you're diagnosed.”

Ms. Landro: Right. Of course, everybody has to do that now.

Ms. Zammett Ruddy: I always guide people to LLS. How many times have I called the people at LLS to say “I have a friend who was diagnosed. She lives in San Francisco.” Connecting them. We are curing more people. We are getting people to that next step, so talking about it right upfront—I remember being in the doctor's office, my mom asking about kids. I was so embarrassed that she brought it up but here I am 14 years later with three kids. I think it's presenting the whole picture and talking to patients not just about curing the cancer but also about the whole life and what could come next.

Ms. Landro: Exactly, the collateral damage that Dr. Love talked about, for a young woman diagnosed with a blood cancer and facing a transplant or massive doses of chemotherapy. I lost my fertility. It's no secret. At the time they were just beginning to offer IVF. Now they can offer to save ovaries. I think there's more of that collateral damage that people are thinking about. Let's think about that life afterwards.

Dr. Love: I would ask that as we've got all these new exciting approaches and new exciting drugs that we really do collect true patient-reported outcomes, not just the side effects we think are going to happen, so that we can also do precision medicine on the collateral damage. I'm sure that there are single-nucleotide polymorphisms (SNPs) or something that will predict who is going to get peripheral neuropathy. We really haven't put much science into looking at that because not enough people have lived long enough. But now that we're having all these successes, we really have to pay attention to that as well.

Dr. Ybarra: Expanding clinical trial opportunities is key because right now too few people think about and enroll in clinical trials. That may be a part of the setting where you're getting your care but there are a number of clinical trials that do happen in the community. So that is an opportunity. And, to Dr. Love’s point on patient-reported outcomes, that's definitely something that the industry is very interested in integrating earlier in the clinical trial process.

On the back end, where we are worried about value and delivering high value care, making sure patients are getting the right value; making sure that we're measuring that, and we have quality measures that reflect value that actually matters to patients. It is really interesting to think about when I ask my patients, what do you want to get out of today's visit? It is a different setting in the emergency department, of course, but it's always eye-opening to see what it is people are looking for.

Dr. Love: It's never what you think.

Dr. Ybarra: It's never what you think. Absolutely right.

[Addressed to Dr. Conti by audience member: What should be done about oral parity when it comes to the cost of medications?]

Dr. Conti: It's clear that patients are facing very high copayments attached to oral cancer drugs, including those that are treating multiple myeloma and other blood cancers. A number of states have passed oral parity legislation to try to reduce the costs that patients are facing out of pocket. However, there's some perversity attached to that. Some of the states did not pass legislation that made sure that insurers didn't raise the prices that patients face for both oral drugs and the infused drugs. Some states had the forethought to actually craft legislation that did that. Unfortunately, right now for many of the drugs that are treating blood cancers, the states are very uneven in what they guarantee in terms of affordability to their patients.

Dr. DeGennaro: This is an area that LLS is very concerned about and very active in. We've been very active in the states that have passed the proper legislation making sure, in coalition with other organizations, the right tenets are being brought into the legislation at the right time. We've heard a lot about the development of new oral therapies. In an interesting way, we're getting to the point where someday the pharmacist will be the frontline of cancer care as we advance those oral therapies. It really speaks to getting the legislation right and building the business model correctly so that patients have access to those drugs.

Dr. Conti: I agree, and it's entirely possible that pharmacists are actually on the frontlines of thinking about this financial toxicity issue and what to do about it. Thinking creatively about how we can actually use that point of care to assess which patients are actually having difficulty and what resources are out there is an important part of the solution.

[Addressed to Dr. DeGennaro and Dr. Byrd by audience member: Is there something that's come back from the FDA indicating that, as you test precision medicine therapies for AML, that they would consider an approval after a phase II trial with 10 or 20 patients? To Dr. DeGennaro: What, if anything, is LLS doing to try to speed that regulatory process, and what are we doing to support precision medicine for AML?]

Dr. Byrd: The FDA, in the talks that I've had with them, has said that they want to move good drugs forward to approval as quickly as possible. The reason I think— and this is my opinion—that a lot of drugs have failed in AML is because they have very modest benefit and a lot of toxicity. The FDA has shown in a lot of other diseases when you have drugs that are very targeted, where you don't need a statistician to tell that it's a very active drug and it beats the pants off of everything else, the FDA does want to move those forward. It's not just in AML. I believe it's in all cancers, blood and solid tumor.

Dr. DeGennaro: LLS has been at the forefront of precision medicine since the mid-1990s. Someone mentioned Gleevec being the first among precision medicine approaches. The development of that drug changed the paradigm of how physicians and scientists think about treating cancer. Suddenly you could use a drug to attack the cancer and leave the good cells of the body alone. That's precision medicine. We've been at the forefront of that, and it's actually heartwarming to know that today, we're beginning to apply those same tenets to many other blood cancers and, as was just mentioned by Dr. Byrd, to many other forms of cancer as well.

With respect to the FDA, the role that we're playing is as educator. We can't influence the FDA nor should we, but we can provide, as a third-party, neutral, credible, up to date information about the state-of-the-art medicine and science in the blood cancers. And frankly, the unmet medical need that patients face. What are the patient issues? The FDA, I'm very pleased to say, has been very open to

meeting with us, gaining that understanding from us, and, in fact, even meeting with patients through us as well, to hear directly from patients about what their expectations are.

[Addressed to the panel by audience member: I'm a survivor of NHL with lymphoma. I was on two vaccine trials and failed in the early 2000s but I am still alive thanks to rituxan. At the table today is every representative except the federal government. In the team approach, what can each player here do to increase the cohesive effort to promote clinical trials? With only five or ten percent of trials (filled), there's got to be a way to incentivize trials, maybe a government contribution, tax benefits, pharma contribution, academic contribution.]

Dr. Love: As a former practicing physician, I think it's the physicians that are the barrier more than the patients because when you talk to patients they're often very happy to participate, in my experience. It's the physicians that don't want to bother, that it's easier to just do things the way they've always done it. Or they're afraid they'll have to lose the patient to another center that's doing the trial whereas they could keep doing the same thing. This is certainly true in breast cancer, and I would bet it's also probably true in the blood cancers as well. We've focused a lot on educating the public, and they're pretty far along. But we haven't done as much in educating and figuring out ways to incentivize or to somehow get the physicians into the pool.

Dr. Byrd: I think it comes back to what we were talking about, costs in value-based care. You're looking at the numerator to denominator of all patients. If you look at patients that are cared for at comprehensive cancer centers down to people in private practice, the frequency of patients going on clinical trials goes down and the outcome—survival—of patients, as measured by the gold standard, goes down. There's been published work on that and the complexities are many. For the doctor that's in private practice, it takes a lot of time to put somebody on a clinical trial, to counsel them, to fill out the toxicity forms, to see them for their extra visits, to meet with the monitors. And in our clinical trial system there's not enough funding for that. Again, I'll come back to LLS. They support clinical scholars that pay people that want to be focused on putting patients on clinical trials. It's part of their salary to facilitate their ability to do that. The doctors have to feed their families as well, so it's a very complicated issue both ways.

Ms. Landro: Certainly, I will say that looking at clinicaltrials.gov, years ago you could never find out about a clinical trial on your own. You can go online now and actually do some really sophisticated searches. Now, I know not all patients are doing that but if they could find a way to get that word out there a little more I think that would give people a little more self-advocacy.

Dr. Levine: I'll just put in one plug again for LLS that maybe we haven't talked about, and it's something that you asked earlier, about how to navigate the system. One aspect that LLS is probably at the vanguard of in cancer medicine is that they have people who sit at telephone banks whose job is to actually help patients find trials and doctors. There are very few other cancer specific foundations who, on a free basis, have people sitting waiting to help you go through that process. I think one thing we need to do as doctors and patients and foundations and pharma is get that message out there.

There actually is an incredibly robust infrastructure that LLS has been providing for a long time that is being utilized by many but could be utilized by many more. I think that patients need to understand that they have many options. They have many people who actually are experts at navigating the system, who are waiting to help them. I think the more we can do to get the word out about that aspect the more the system benefits.

Ms. Zammett Ruddy: For what the patients can do, I think that joining clinical trials when you can is important. I know that a trial always sounds like it's your last chance, and it's not like that. There are so many trials out there that are not just because everything else has failed. In my experience, I was ready to join this trial a year ago. This is a trial where you just stop taking your drug. It's very simple. In order to get that through at Memorial Sloan Kettering, it took a really long time. I could have gone off my drug with just Dr. Mauro; I didn't have to do it through a trial setting. But it was important to Dr. Mauro and it was important to me as an advocate, and so I did it. There's more visits. There's ridiculous surveys that were definitely not created by patients. "Can you run ten miles without difficulty?" I'm not sure how that's important.

But I do think it's important to spread the word about trials and to join them when you can. They're not scary. I was in a trial for the first 18 months. I loved that extra care and having people ask me questions constantly and wanting to know all of that. Now, I don't want to answer those questions as much as in the beginning, but I think just talking about it as much as you can is helpful.

Dr. Love: One of the things we've done in breast cancer is we have an Army of Women (AOW) through my foundation. It's about 400,000 people with and without a breast cancer diagnosis, who have signed up to get e-mails about studies. Researchers come to us with their studies. We charge them our cost. Our scientific advisory committee reviews the study and if it is appropriate we send a summary of the study out to everyone in the AOW. We don't match anybody, but send it out to everybody because sometimes the study is in Oregon and you're sending it out to somebody in Florida but their sister lives in Oregon or their friend. Every time we send out the studies they virally get sent out further. We've been very successful at recruiting for a lot of research and also letting the public know what research is being done. By sending the e-mails out to everybody, everybody hears about the different studies that are going on and realizes that things are happening. There are ways you can increase the knowledge out there and have people be more inclined to participate in studies.

[Addressed to the panel by audience member: My question goes back to the access issue. I live in one of the 11 states that haven't passed parity legislation, Pennsylvania. How would you bridge the gaps between legislators who want to attack cost from the bigger perspective and patients who need access to treatment? And with generic or biosimilar versions now starting to be approved, is that going to play a role in how this moves forward?]

Dr. Ybarra: Medicines are unique because they do go generic. You have a medicine on the market that's transformative, and after a certain period of time it's going to go generic. There is always that market change.

I want to make sure everyone knows we do work collaboratively on a policy level, and we're trying to do more. Particularly in this time of intense change, where the system has changed fundamentally in the last five years and we've had an incredible change in the science, our advocacy effort is to really make sure that patients have access. And it's not just legislators, it's also advocating and working with the Centers for Medicare & Medicaid Services (CMS) to take a hard look at some of these formularies and make sure that patients have reasonable out of pocket costs and that there aren't formulary design issues formularies that create barriers to access, not just for cancer but even for a disease like HIV.

There's obviously more work to be done on the advocacy front. It's something we're working on to the extent possible, we are talking about this value driven healthcare system. And that is going to mean having conversations with payers moving forward.

Key Points of Consensus

Consensus emerged from the diverse group of panelists around the collaboration that is occurring across the ecosystem between scientists, academics, pharmaceutical companies, regulators and advocacy groups. Panelists also focused on the big role precision medicine has played and will continue to play on the development of cancer treatments. Overall, the panelists recommended that the following actions be taken to advance blood cancer research, treatment and advocacy:

- Collaboration must continue across the board in order to advance the development of treatment and support patient care.
- A focus on precision medicine will continue to positively impact the development of cancer treatments.
- There needs to be a continued focus on the issue of patient access and affordability.
- Enabling patients to assist in generating patient reported outcomes will help with overall patient care during and following treatment in order to improve quality of life.
- Venture philanthropy will continue to be an important part of the drug development ecosystem.

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