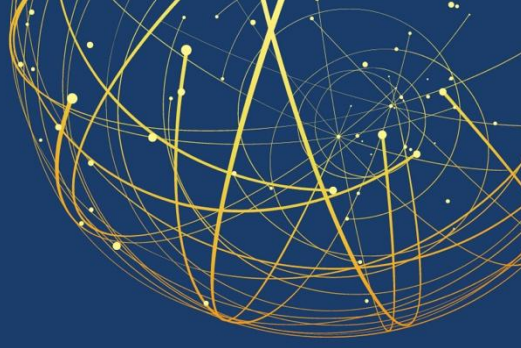

PART 2: WHAT WILL SUCCESS AGAINST CANCER LOOK LIKE IN 2035?

Alice Park 00:02

Good afternoon, everyone, and thank you for being here. We're going to really pick up, I think, where the previous session left off, and that is really to talk more deeply about what cancer care will look like in the next decade. And very excited and looking forward to this discussion, because we have a nice representation, I think, of the major stakeholders, of the folks who will really be shaping what that care will look like, from the research side to the drug development side to the patient and clinician perspective. So, I want to jump right in and ask each of you, since we're talking about cancer in 2035, what is the one thing that you would like to see in another decade happen in cancer care, and to be a reality? Maybe we'll start with you, Kent.

Kent Bradley 00:57

Well, I will start first off with the recognition that the work that my colleagues are doing, and others, in the diagnosis and treatment of cancer, earlier diagnosis and then the innovation around treatment is phenomenal. But I'm a preventive medicine physician, so I have to go through the lens of prevention. And I think from a layered approach of primary prevention, that's the highest leverage point and the greatest return, and it's what we all want is to never have a cancer cell ever be formed. And I think 10 years from now, I think we're going to recognize that there are a lot of markers and data that we need from a genomic and biomarker to understand the inflammation and the pathways, so to get at cancer from a primary prevention. The secondary prevention, when we've got an early diagnosis and therefore a greater opportunity to create leverage and treatment, is where a lot of the effort is, and rightfully so. The $200 billion cost of cancer—and we need to continue to grow that effort—so, in 2035, I think that is we have made multi-cancer detection mainstream. But then the missing gap is really around tertiary prevention, and that is there are 18 million Americans that have recovered from cancer, and yet we still don't have a comprehensive understanding of how to personalize and provide precision care for them from a nutrition foundation so that we support their inflammation. So, my wish would be in 2035, just like cardiac rehab is mainstay for somebody who's had a heart attack, that there's a comprehensive program of support,

nutrition that's guided by data and proper intervention at a foundational level to tackle that tertiary prevention.

Alice Park 03:03

So living better with cancer because it was diagnosed earlier-

Kent Bradley 03:05

Or never having it.

Alice Park 03:06

Or never having it to begin with. Okay. Jay?

Jay Bradner 03:09

Well, Kent, I love your answer. And I will say that I hope we have a chance to talk more about what cancer prevention looks like if you were to bring the power of precision medicine to bear on precision prevention. It would look very different.

Alice Park 03:24

We will. We'll talk about precision medicine.

Jay Bradner 03:30

But having covered prevention beautifully, it turns out there's a lot we don't know about cancer. I'm a cancer doctor and a cancer drug hunter. And we're always learning and learning from each other around what are the Achilles' heels of cancer? Can we make a medicine targeting the Achilles' heels? But there's a group of targets that we've just known about for 30 years need medicines, and they remain as yet undrugged. They're called undruggable targets, believe it or not, in our field of science. My least favorite term in all of science. And it isn't that they can't be drugged, it's just that we haven't as yet conceived of a way to drug them. Until a few years ago, when we in Amgen and others have found that if a molecule can't bind to a drug target, c-MYC, that causes most cancers, c-MYB, that causes so many blood cancers that I take care of. If there's no pocket, how do you make a key for a protein that has no keyhole? And so, the concept that we've come up with are called molecular glues, that you can take a protein over here that's not even involved in this biology, bind a drug to that protein, and in the moment it binds that protein, it grabs the target that you're after, and you glue—

Alice Park 04:37

—Which is the tumor cell.

Jay Bradner 04:38

Yeah. And you glue this undruggable cancer drug target to another protein and destroy it or preoccupy it. And the very first medicines are coming out of our pipeline, and others, of this nature. We call them induced proximity medicines. And so, I'd like to see 10 years from now the surrender of all of these legendary and challenging, historic and undruggable targets finally surrender to discovery science.

Alice Park 05:05

So, no more undruggable targets. What are they called? IPMs?

Jay Bradner 05:09

Well, there are—it's very interesting you mention that.

Alice Park 05:11

Needs a better name, I think.

Jay Bradner 05:12

Yeah. No. They go by a number of names. One flavor is called molecular glues.

Alice Park 05:18

Okay. That works.

Jay Bradner 05:18

Another are called induced proximity medicines.

Alice Park 05:22

Okay. I think molecular glue works better. All right. Stephanie, from the patient advocacy side, what one thing would you like to see in place by 2035?

Stephanie Kauffman 05:31

Collaborative velocity. And really, it's how do we bring everyone together with putting siloed agendas aside? So how do we get an area that we're seeing great momentum around is patients coming together. They're pooling their resources, they're actually pooling data. They are changing the conversation of where research priorities are at. And so how do we bring first that patient-centered outcome and the collaboration for patients? We bring in phenomenal industry partners, our researchers, our clinicians across the whole research continuum, as well as private capital. And how do we do that truly in the way that we are centering on patient outcomes, patient survival, better early detection, creating better consortia, looking at more pre-competitive data sharing in a way that's maybe not happening at the rate that we would like to see it? I also think in terms of velocity—the way that health care is moving, and certainly what we're seeing with AI—is a velocity in terms of how much data that we have at our fingertips. But at the same time, how do we make that funding velocity happen? So that collaborative funding, shortening the time on funding grant cycles, making some of those opportunities more milestone-based, shortening those funding cycles in a collaborative consortia, and getting funding and private capital into researchers' hands that is feeling very collaborative without silos, so that we can ultimately impact patients' lives in a faster way because cancer speed is survival, and we need to get there. And I think we have a lot of exciting momentum happening for that over the next decade.

Alice Park 07:15

Okay, so working better together.

Stephanie Kauffman 07:17

Absolutely.

Alice Park 07:18

Björn, you bring a perspective from outside the United States, an area, Saudi Arabia, where that's not historically been a hub of medical and health information, trials, research, things like that. But that's changing. So, tell us what you'd like to see.

Björn Zoëga 07:40

Yeah, I would like to see that we would not be in end of our journey, but still ongoing the journey that we have started at our hospital, and taking care of the cancer patients, the most difficult ones, 25 percent of all cancer patients for Saudi Arabia in our institution. And that might not sound much, but it's still really much for a country with 34 million inhabitants. And also, it's a young country, so the median age today is 29 years old, so we know the cancer wave will be coming. So, what we are trying to do is to find the way to—and I hope we will not be, like I said, the end of the journey—but on our journey to make the newest treatment available in collaboration with everybody else, the industry, smaller companies, bigger companies, and scientists. We're trying to build the way to collaborate, not to buy stuff. And in that way,

also, particular interest in using all this data that is out there. I've had some background in genomics and genomic data specifically, and we're really the only institution in Saudi that has any genetic data to talk about. And so how do we use it? I hope personalized medicine will have come that far that it's usable, not only for cancer, but for all other diseases. Today, it's a bulk of information that I cannot see that we have managed to take all these billions of letters and put them in a usable way. We have those silos of things, particular cancer or cancer type, that we're trying to use it in that way. But how can we use it as a whole? And we've got some really good ideas. We're working on some really good data management in collaboration, international collaboration, because—I think, like you said, we need to break down the barriers—because it's a win-win situation for all of us. Doesn't matter if you're big pharma, small pharma, institutions, societies, and it's the patient in the end. That's why we're all here. That's why we're all here. It's so simple. We're so blessed being in health care because we know why we're here. I look at some of my friends that are in banking. So why are you here, guys? Oh, we're making money for somebody else. No, we are here for the patient.

Alice Park 10:25

Okay, so unlocking that untapped potential of the data. It seems from your comments that we can sort of divide our conversation, I think, into looking at early detection, prevention, and where that's going to lead us in a decade, and also drug and drug development, new treatments. So, let's start with early detection. Kent, what does that mean? And as far as when we start looking at innovative ways to detect and even prevent cancer, we've got AI now, we have advances in imaging, genetic testing. A lot of things are sort of bubbling up now, and we're on the verge of having standard liquid biopsies, blood tests that can detect signs of cancer. How do you see all of those coalescing in the way that a primary care physician in 2035 is going to approach helping someone to prevent or detect or prevent cancer before it happens?

Kent Bradley 11:28

Yeah, I think one of the biggest challenges, quite frankly, that maybe AI can support is educating the providers. The pace of change, the amount of tools in the toolkit are expanding for early detection, but the knowledge around and the appropriate use of them has not. But I, again, go even further upstream. And I think when we talk about detection, we think about the many ways in which we can detect the presence of cancer or early signals. But the earliest signals really come from one's inflammatory situation, if you will. Metabolic risk and inflammatory load, one could argue, is even preceding the issue. And so, I think part of the opportunity for us is to begin to also educate the provider in how that plays a role in overall health, but specific to cancer. And to do that, we have to have a better understanding of the interplay between genetics and how we process, as well as a better understanding from a nutrigenomics perspective as well. Not precision medicine, genetic cancer detection risk, like we've thought of it more often, but what is the predisposition for us from a genetic perspective to have increased inflammatory risk, as an example. And couple that with biomarkers—an expanding list of biomarkers that people can then understand beyond what is typical today is just a CBC and a comprehensive metabolic panel. That is insufficient and should be changed as we expand the tools in the toolkit for understanding our body and how our body can be optimally supported through nutrition, supplements, and other things that we could be doing.

Alice Park 13:26

And so you're talking about a real mind shift, because I think now when we look at cancer care, it is reactionary. It is in response to once you see symptoms, once you see signs of cancer, and we want to get to the point where our thinking is that we need to be able to look at that panoply of risk factors. It could be environmental, it could be behavioral, it could be molecular, could be genetic. But we have to get to that point where we're in that mindset. Stephanie, from the patient perspective, how important is this for the patient community, and how much is this trickling down in terms of the understanding of the importance of investing in this and focusing on prevention, early detection, while people are living with cancer now? It's easy, and I think I've spoken to a lot of doctors who say they're very eager to look at prevention, look at new treatments, but they're often pressured by saying, "Well, what are you going to do for the patients who are dying and suffering right now?" So, I'd be curious to get your perspective on that and how you shift that understanding or start prioritizing early detection and prevention.

Stephanie Kauffman 14:38

No, it's a great point. I'm currently in the melanoma space. I've been in the breast cancer space, and if you look at those portfolios of research, you have maybe a small percentage that's around prevention and early detection, and most of it is really, 80 percent is focused on treatment portfolios, right? How do we take care of the patients who've already been diagnosed with this disease? The case of melanoma is really interesting because we actually, for 90 percent of melanomas, there's some rare subtypes. We actually do know what causes melanoma for 90 percent of melanomas—it's UV exposure. Increased additive UV exposure through the years—and so, for us, there's a couple of things that are at play. Number one, early detection. If you're able to detect a cutaneous melanoma, so that's melanoma directly on your skin, it's a mole that's grown out of control. For the most part, it's a 99 percent survival rate after five years. If it is detected late and you go into advanced cancer, which is probably true of a lot of cancers, that survival rate drops down to 35 percent. Melanoma is a very fast-moving cancer. So, one of the things that we're looking at is, for example, 40 percent of the United States live in what we call dermatology deserts. They do not have immediate access to a dermatologist, and they're going to have to travel potentially several hundred miles, and it's going to take five to six months to get in to see a dermatologist because there's a shortage of dermatologists. So how can we, number one, utilize AI? We're not there yet, but you could use your cell phone, take a picture of something that looks really suspicious on your skin, have it sent to a virtual pathology lab. They can determine whether or not this is fine, or we need to triage and get you into care immediately. How do we then take some of those same tools out of dermatology and actually arm primary care physicians and PA staff to give that better access of care? I also think, within that, it's also for us in the melanoma space, it's around better public health messaging on that melanoma is a fast-moving cancer. It represents 80 percent of the deaths within the skin cancer ecosystem. It moves fast. It turns metastatic very quickly. So, we also need some public health messaging as it relates, particularly in our space, on what you can do to prevent a highly preventable cancer, which is not the case when we think about what causes pancreatic cancer and glioblastoma. So I think it's really the two, how do we use technology earlier? How do we create better data and infrastructure and access for patients who may not have it? We certainly see that. And by the way, when we talk about these dermatology deserts, that actually includes even in New York City. On the Upper East Side, you probably have a lot of options for dermatologists, but if you're in Far Rockaway, you may have one dermatologist for 600,000 people. So dermatologists exist in rural communities as much as urban communities, and I think that's one of the areas that we feel we can absolutely make a huge impact on changing the trajectory for those who are impacted by this disease if it's cutaneous. Rare forms of melanoma, such as acral, mucosal, uveal. Uveal is the eye, acral is on the palm of

your hands, mucosal is in the wet tissue areas of your body. That's where then we have to go into what Kent and Jay are talking about, is—how do we unravel the biology of those cancers? But that's where we see a huge opportunity to change the paradigm of cancer care and treatment and the expense that goes along with that.

Alice Park 18:17

And I think we're going to come back to the issue of technology, but as you were saying, technology can play a huge role in that, in reaching a larger audience.

Stephanie Kauffman 18:24

And I think that's got to be one of the new actors, if you will, in our space, is all the data companies rethinking—we're more than health care now. We're data, capital, and infrastructure, and I think we'll need to continue to see data companies really lean in on that space with all of us.

Alice Park 18:43

Yeah. So, Björn, as someone who runs the largest hospital in Saudi, how are you looking at resources and personnel as far as when it comes to cancer? How much is devoted to prevention, testing, messaging, as Stephanie is saying, versus treatment?

Björn Zoëga 19:01

So I will start with saying—come and look in Saudi. We have solved this thing—that most of the melanoma suspicious things are run by the primary physicians because we are a very big country, and we cannot send the patients. And they're sending this digitally to the virtual pathology that we have, and it's only when that is needed that they come to us if there's something needed to really be done, sort of a big thing. And it's not only cancer. So about 25 percent of all our visits are virtual, that we have contacts with our patients. We're talking about over half a million virtual visits a year done in cooperation with primary care. Otherwise, we won't have enough people to do this. And we're supporting with education in different ways for the preventive care in other ways as well. And we know that it's not only Saudi, it's not only Europe or America, whatever. If we don't work differently with both the preventive care and the treatment, then we'll run out of people to take care of these patients, not only cancer patients, but others as well. So, we have to think different. Like Steve Jobs used to say, "Think different, not differently." So, we have to think different, and we're starting doing that, and I sometimes say in these things, how do you allocate resources? And the future is now. We can see that with all these new treatments that are making such a difference in cancer and other things. The future is now. We cannot wait. The bus is moving. So, we have to do things differently. It's the hardest thing that you can get a physician to do, is to work in another way than they were trained for 10 years ago, five years ago, 20 years ago. It's the hardest one to do, so we have to start doing it.

Alice Park 21:20

But are you seeing a difference in the new generation of doctors that are being trained? And we're already seeing it everywhere, I think, that most of them are much more comfortable with ChatGPT, with digital health, virtual visits, things like that. Are you seeing that difference in the next generation of doctors?

Björn Zoëga 21:38

Well, I think I've seen it with most doctors, of that they are embracing anything that saves time or gives them more time with the patient. We've seen what a revelation the ambient listening has done, which is AI to a certain degree, at least, depending on what kind of technique we're using in that one. It has been a revelation and also a revelation for the young doctors that don't work as many hours as we, the older ones, have been used to. And for many reasons, and also if we push them to work too much, they are not as, well, at least talked about this, the burnout rate and everything else that will go up. So, yes, we see that they are just part of the society, and the society is changing with these types of things.

Alice Park 22:37

So Jay, let's move on to drug development now. You talked about this molecular glue. As you look toward the next decade, what technologies or platforms that may be still a little bit early for prime time right now are you excited about that you hope to see mature in the coming decades?

Jay Bradner 22:59

Well, I'm going to answer your question, but I want to circle back to this prevention idea because I think there's something very exciting happening at the convergent innovation hub of biology, genetics, medicine, and artificial intelligence that I think can solve a lot of the challenges or contribute to the solutions that we're talking about. To answer your question, molecular glues, small protein molecules that bring immune cells and cancer cells into proximity, molecules that do more than just one thing, bind and inhibit or bind and activate, but that short-circuit disease processes by bringing pathways together and changing inflammatory responses or cancer responses. These are high times for being a drug hunter. We have cellular therapies that can cure leukemia and lymphoma that probably can be replaced soon by injectable devices. It's a very exciting time to be a drug hunter because we have so many tools. And because we have so many tools, often the rate-limiting step is the awareness of the target itself. And as we're talking about prevention, and something you said, Steph, really resonated with me, which is how little attention prevention is receiving. How little attention at the primary care provider level, which is really where it's achieved. How little resource from federal funding. How little resource in private funding. Biopharmaceutical companies must spend $300 billion a year on R&D. It's a fraction of that that goes to prevent diseases. Disease interception is the norm. I'm proud to work at Amgen, where we're very, very serious about disease prevention. With medicines that prevent heart attacks by lowering LDL-C, medicines in a late stage of clinical development right now that will hopefully prevent heart attacks by reductions in Lp(a), medicines that promote healthy bone in order to prevent fractures in post-menopausal osteoporotic women. And we have some ideas about cancer. And I think that what I've learned over the last, I don't know, 30 years studying and drugging cancer targets is that by the time you have a cancer, it's so

challenging, it's so heterogeneous. You give a medicine—it responds, it adapts, it grows. You give another medicine—it responds, it adapts, it grows.

Alice Park 25:18

It also changes the body, right?

Jay Bradner 25:20

Correct. It changes the body, and the cancer changes in response to the medicines.

Alice Park 25:23

Right.

Jay Bradner 25:23

And because cancer biology is so mature, most of the targets that we make drugs for come from the study of cancer biology or the genetics of the cancer itself, which are different than the genetics of the body. And those are a great source of ideas for how to treat a cancer. But they're not good source of ideas for how to prevent a cancer. Where do cancer prevention medicines come from? It's often a medicine like tamoxifen that might be used to treat late-stage cancer. And then it's pretty effective, so let's move it up into early-stage cancer. Well, it's pretty effective and well-tolerated. Let's move it up and give it to women who are at risk for cancer. But that paradigm breaks down because many cancer medicines that would treat a cancer are more toxic than one would take to prevent it. And it turns out the biology of what drives a cancer is different than the biology of the cancer itself. Now, in cardiovascular medicine, we've known this for years—and we take experiments of nature, natural variations of all of us here in the room today at population scale—and we say, "Show me all the individuals that have an early heart attack." And you say, "Oh, a lot of these people have an elevation of Lp(a). Well, let's make a drug that drops Lp(a)." And we're working on that. Then we ask a second really important question. "Show me all the genetic changes, the variations, that protect people from ever having a heart attack." And we find PCSK9, and we study PCSK9, like Simon Jackson in our labs, and we make an antibody against PCSK9, and it drops PCSK9 levels in everybody irrespective of whether you have the variation or not. And the genetic protection is now conferred on everybody with the medicine. So as a leading company in the study of human genetics with three million genomes right now in a server in Iceland—where I know, Bjorn, you hail from—and where we perform our genetics research with an NVIDIA SuperPOD supercomputer and some of the smartest geniuses in the field of genetics, we're poring over an increasingly large amount of human genetic information to ask questions of the experiments of nature. What protects against obesity? Low GIPR. Okay, let's make a GIPR antibody. We've asked that question about cancer, and we find genes that prevent people from developing a cancer that aren't anywhere in the cancer literature. One of these genes is called PPP1R15A. There's only 16 papers about this gene in the title. None of them talk about cancer prevention. And it turns out, if you're so lucky as to have one bad copy of that gene from your mom and a good copy from dad, your risk of breast cancer is reduced by 54 percent. Yet by the time you have a

breast cancer, that gene is not an interesting target. So, we're very interested to look at these experiments of nature and natural genetic variation—and to collaborate with institutions serious about sequencing their patients, countries serious about sequencing their citizens—and asking this question: What are the genes that keep people from getting cancer, and can we make medicines to confer that protection on everybody? We're going to find different genes. And artificial intelligence turns out to be really important for this because you probably heard and you've probably experienced that AI can see patterns that the human brain can't comprehend or recognize.

Alice Park 28:48

It can find the PPP1R15A, right?

Jay Bradner 28:50

Exactly. And when it's one gene causing one effect, we're pretty good at that. That's logistic regression. That's simple statistics. What if it's a constellation of three genes collaborating to protect? The math breaks down. And so now going back and asking these questions, what protects against heart attack, obesity, the serious diseases that we care about at Amgen? We're using artificial intelligence to guide us to new insights and new targets to prevent disease as really the best way of never having a disease.

Alice Park 29:21

So, I'm glad you brought up the issue of data because both Stephanie and Björn, you talked about that. And Björn, I want to go back to you and ask you about the data sets that you're building there, because I've also spoken to other people in the region who have noted that, for example, the world's genetic databases, the ones that most researchers turn to when they test drugs, try to develop drugs, look for patterns, are really based on Caucasians, and really don't involve many Middle Eastern ancestry genomes. So, tell me a little bit about how important it is to have data sets that are more diverse or, in some cases, when is it more important to have one that's a little more localized?

Björn Zoëga 30:07

Well, this is one of the things that we are sort of moving ahead on. Because of cultural issues and other things, the genetic composition in the Middle East is, I would say, completely different. It's very different. It has probably a big effect on how cancer drugs and other drugs work. This hasn't been studied. We're trying to study as much as possible about that. This also leads to that in the Middle East, there are diseases that are, in other places, called rare diseases that are not rare there because of consanguinity and other reasons. So, it's an opportunity to learn more. But that is something that we need to collaborate, be better on that. And what we are really now is, we are reactive in that way. What we, as the hospital, are doing is collecting on those that are referred to us with the diseases, or every cancer patient gets this done, and we have the data for that. But it's sort of how you're going to use it and, like I talked about earlier, is I think the jury's still out there, or finding the right way. And I think, you talked about it, we have the great opportunity of AI. But that only as a—I wouldn't say co-pilot, somebody sort of stole that word—but as an

assistant to us to sort of help us to work on these things and make life easier in many ways, not as the driving partner in that one. But I think I'm very optimistic and ambitious for us that this will now be listened to, and we will maybe get some more ideas to work with when we see that, both on the prevention side, but also on when you're finding new drug, new targets, whatever. It just needs to be done more of it.

Alice Park 32:25

Right. And Stephanie, patient advocacy groups have really played an increasingly important role in defining research agendas, goals. You talked about collaboration, the importance of collaboration, which is what you'd like to see occur in the next decade. Which stakeholders do you think are missing in that collaboration, in that grouping, that you would like to see join or have a bigger voice?

Stephanie Kauffman 32:52

First, patients. I'd like to see more patients get involved in their care, more patients getting involved in the research agendas and understanding how powerful their voice can be. So, we're very fortunate at the Melanoma Research Alliance. We have a number of patient groups across what we do, and particularly, I would tell you, within the rare melanoma space. We have now really brought about a bigger patient voice to drive research for rare melanomas, that were basically not researched at all. And those rare melanomas actually proportionally impact all population types. So, I think that that's really important. So, I think the patient voice. I would also like to see media and the news have a bigger voice in terms of pushing out trusted information around what is happening in research in cancer and prevention. I'd like to see the tech companies come to the table. One of the things we've discussed is, I think about certainly patients that may be in my age category that maybe address their care in a certain way as opposed to maybe Gen Z populations. And the reality is, is Gen Z gets the majority of their health information now not from maybe those traditional media platforms that we all did, but they're getting it off of social media, and in particular, TikTok. And so, I'd like to see those players come to the space on how that we can provide better prevention, education, treatment information in a way that we're not seeing today.

Alice Park 34:27

Be partners with health care professionals and health organizations.

Stephanie Kauffman 34:34

Absolutely.

Alice Park 34:35

Yeah.

Stephanie Kauffman 34:35

And we're starting to see a little bit of the evolution of that, and we certainly are seeing it within our own patient community of using social media. And I think lastly, we still need for academia, industry, nonprofit organizations with the patients and industry thus large, as well as government, to all come together and to be in a room to solve for those problems. And we get it, but it still feels a little fragmented. I feel like there is more collaboration now, but I think all of us would like to kind of see everybody just get into the room, put what we need aside ultimately for the patients, and we also need to do that more internationally than what we do today.

Alice Park 35:21

Okay. Want to now go down the line and ask each of you about something that's been a buzzword for years now, which is precision care, personalized care. And it's been particularly important in cancer. So, Kent, I'd like to start with you and ask you, what role do you think precision care will play in cancer in another decade, and how do you think that will balance with more kind of universally applied, either screening, testing, treatments?

Kent Bradley 35:44

Yeah. When you think about how public health infrastructure focused around prevention, it was at a layer of knowledge that was difficult for people to embrace because it wasn't about them. It was maybe about age group, gender—those kinds of markers. For me, precision care means knowing, not guessing, and knowing about me personally, which also plays into the health belief model. The reason why people don't take action is because they don't think it actually pertains to them. So, I think knowing is a health activator, and I think precision care must also include precision health, not just care. And precision health means I know something about me, and I have ability to act on that from a genomic biomarker perspective. And then that will begin to turn the tide on the ability to now care in a more unique way.

Alice Park 36:49

So we build on those personal health records that we have and really turn them into something that becomes a foundation.

Kent Bradley 36:56

Yeah. But I would expand on that. Because if you care about somebody, you also take into effect their agency and their goals and preferences. So, knowing that aspect interplayed with their genomics and their biomarkers, you can provide the proper guide. And I think increasingly, the role of the health practitioner is one of a guide, is to be that of a pacer, if you will. I run marathons, so they come alongside, they make sure that you stay on target, that you're hitting your windows of your pace. They're pacing you. They're not

cajoling you, telling you, and you let their agency come full bloom by giving them the knowledge they need to make the choices.

Alice Park 37:44

Okay. Jay, from the therapeutic side?

Jay Bradner 37:48

It's fair to say that we're in the era of precision medicine from a drug discovery and a drug development standpoint. And there are some, fewer than before, conspiracy theorists like my sister, who believe that, oh, companies don't really want to know who the patient is that would best respond. They want to give the medicine to as many people. Man, nothing could be further from the truth. When we know exactly who the patient is that might respond to this medicine, we have a bigger impact for that patient. We could do a smaller and more effective clinical trial, get through the regulatory process faster, look a doctor right in the eye and say, "This is the patient that would most benefit from this medicine." But can I tell you, it's really hard to know. Some of our most important medicines we've made recently, we have a medicine for the most aggressive form of lung cancer called small cell lung cancer. And this medicine called tarlatamab grabs the immune cell with one arm, just like the melanoma field taught us, and then it grabs the lung cancer cell with the other arm, and it brings them together, forming an immune synapse, and the cancer is destroyed. 100 percent—well, 90 percent of patients will have the protein on their surface, but only 40 percent respond to the drug. And so, we have this medicine now approved for use, and it's become one of the most important medicines in small cell lung cancer. But back in Thousand Oaks, there's a lab bigger than this room full of people trying to figure out what is it about that 60 percent that have the protein on the surface but aren't responding as dramatically as the others. Because when we can learn that, we know who to tailor the medicine to, but biologically, it will open a door to a medicine that we might use in combination to potentially have 100 percent of patients respond.

Alice Park 39:34

Okay.

Jay Bradner 39:34

So precision medicine is our current everyday way of life. It's our highest aspiration, and I think we quite variably but often very meaningfully deliver on that.

Alice Park 39:47

And it's the future. Okay. Stephanie, from the patient perspective, are patients appreciating the importance of having individualized therapies or tailor-made therapies?

Stephanie Kauffman 39:55

Oh, absolutely, because they feel like they're being talked to as a person of one as opposed to patients of many. And I think certainly in our space, what really has so much momentum and excitement around is immunotherapy. And I think it's such a golden age where we are, and Jay and I were talking about this, regardless of all the things that we know that are surrounding cancer research right now, there's such a golden age. We're seeing so many new therapies that are addressing things like BRAF mutations, NF1 loss in a way that wasn't even being talked about 10 years ago. And I think immunotherapy, neoantigen therapies, what we're seeing in CAR-T cells and T cell engagers, and just even two years ago, tumor-infiltrating lymphocytes—where it's basically taking the white blood cells out of a tumor, replicating those copies, putting it back in—and we're having patients that were basically told, "You have three months to live," and now they're no evidence of disease because it was really personalized to what their immune system was doing. And I think we're going to see tremendous momentum for patients, and there's a lot of excitement within the patient community around that.

Alice Park 41:04

Okay, great. Björn Zoëga, Stephanie mentioned CAR-T cells, and I know that you have been championing a very aggressive and very focused effort there at King Faisal Hospital on CAR T cells and being able to manufacture them there locally and really bring this therapy to more patients.

Björn Zoëga 41:26

Yeah. We've managed to, and are still expanding that, we managed to build our own CAR-T cell lines. We're still in collaboration with others, finding other things that sort of we can produce, in collaboration as usual, and have it affordable, or more affordable.

Alice Park 41:48

Because these are specific to individual patients.

Björn Zoëga 41:49

Absolutely. And they are specific to individual patients. So, I think a lot of the precision medicine is here, but like you said in the beginning, you have to know. It has to be facts. And as we know, in my opinion, the guessing in the treatment of cancer patients is over because many years ago, in my early years, we used to give our patients drugs that worked for 55 percent, 45 percent didn't work, and maybe 25 percent had adverse effects on the cancer. Now we have the opportunity to find the right one that gives maybe not more than 40 percent, but still are not doing damage. So, we are there to a certain degree, as has been described. I think we just need to move on and continue this work. And like I said, this is something we need to do collaboratively. We have to work both with data and then through borders, over borders, through different societies, through different institutions, and with different companies as much as possible. I know everybody has to make a living and everything like that, but still, I think things are getting

complicated—even more complicated when we don't understand the whole system. So, to de-complicate things, we need to work together to get our best minds and not only our supercomputers to do these things.

Alice Park 43:29

Okay. Jay, I'm going to come back to you and play your sister for a little bit—ask you. Obviously, this conversation shows how important the idea and the shift toward early detection, prevention is going to be in cancer, and how that's really going to transform cancer care in coming decades. Is there a business model for a pharmaceutical company, for pharmaceutical industry, that has been built on treating a disease to prevent it?

Jay Bradner 44:01

Yeah. I think we've learned from cardiology that there very much is. I will say it's not for everybody. Rare disease medicines, the path to approval can be studies of 100, 200 patients. Cancer medicines, the path to approval, the expensive and involved process of drug development over many years can be studies of 200, 300 people. Our cardiovascular prevention studies are sometimes 10,000 or 12,000 people. Those are big, expensive, and uncertain studies. These studies will run for four and a half, five years, and they will measure one thing: Do these patients fare better from the standpoint of cardiovascular events? And a cancer prevention study would be an even longer—

Alice Park 44:49

—Because it takes longer for cancer to develop.

Jay Bradner 44:50

So, we don't get that many shots on goal as a society. But I do believe that for the medicines that would really move the needle, there's a business there because there's an impact there. And in our line of work, when we deliver impact on parallel impact in a serious disease, well, there's always a business there.

Alice Park 45:13

Okay. Well, I think we have a lot to look forward to in terms of positive advances in cancer over the next decade. So, I want to thank all our panelists, and thank you.

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