CONQUERING CANCER: INNOVATIONS CLOSING GAPS AND IMPROVING OUTCOMES

Kristen Dahlgren 00:10

Thank you all for joining us, for this—"Conquering Cancer: Innovations, Closing Gaps and Improving Outcomes." This is supposed to, I'm told, run as kind of a dinner party conversation. So for you all—you know—grab a glass of wine. You'll have a QR code. You can ask us questions. And for all of you, feel free to add to the conversation as we're going through so it really does feel like a conversation. This has been called the golden age of cancer science, and to tell you just how much I believe in that moment, my story is that I was an NBC correspondent, never expected to be a cancer and science advocate, and then I was diagnosed in 2019 with breast cancer. After I went through treatment as part of my reporting, I learned that cancer vaccines were in development, and it was that moment for me when I was like, What do you mean? We have this incredible science and it's not getting to patients. So I actually quit my job and founded the Cancer Vaccine Coalition to try and accelerate this science. So I really believe that this is such a unique moment when I first had these conversations in November of '23, doctors said, Kristen, don't say "cure". I now, on a daily basis hear doctors using that word "cure" freely, unabashedly. And I think that is such an exciting time. Of course, none of it matters if it's not reaching patients. So we're going to be talking about that as well today. And so this progress, and then how do we get it from the lab and into hospitals and into homes? So Julian, let's start with you. Let's start with hope. What in this moment makes you the most hopeful?

Julian Adams 01:52

So I'm hopeful about the technologies we may be discussing on stage today, because I think it's the next wave of research, including immunotherapy, the next advent—and I'm glad you said vaccines, because I work extensively in vaccines.

Kristen Dahlgren 02:10

Your team has reached out to me too to see if we can collaborate. So I'm excited.

Julian Adams 02:15

So I my weekend job is, I'm chairman of the board of a cancer vaccine company based in Boston, developing a pan-KRAS vaccine currently in clinical trials for pancreatic cancer. So very hopeful we'll see data in the next few months that justifies all this effort.

Kristen Dahlgren 02:34

So vaccines, what are some of the other things, specifically technologies that—

Speaker 1 02:39

So there, my background is—I spent—I'm trained as a medicinal chemist. Spent my 40 years of my career in pharma and biotech developing drugs and therapies, and my failed retirement was to join the nonprofit world. And I tried to see, you know what—what's the gap between what is academic research going to study and discover and enable? And I know what industry does, and so I look for the gaps. The biggest gap, I think, is in diagnostics. It's a hard business. I'm all in for liquid biopsies. We'll talk—we'll talk maybe about a project we're funding right now. So early detection, early stage detection, and then interception, and interception by multiple modalities. I'm very excited about vaccines, but there are other topics. We'll talk about theranostics and ADCs and biparatopics. And there's a ton of things, I'm sure the whole panel will chime in on.

Kristen Dahlgren 03:45

Yeah, absolutely, and Maddie, I know early detection is something that's important to you. You lost your husband, Patrick, to a rare cancer. Can you tell us a little bit more about him and your experience?

Maddie Musselman Woepse 03:59

Yeah, of course. So I'm Maddie Musselman Woepse. I'm the president of the Patrick Woepse Foundation and the NUT Carcinoma Alliance. I'm also an Olympic athlete, professional athlete. I played on Team USA for women's water polo from 2013—currently—and I am currently in PA school as well. So kind of have this experience in a lot of different areas. And my husband was diagnosed with a really rare and aggressive lung cancer called NUT carcinoma back in 2023, and we are both athletes. He played water polo at UCLA, and he had just completed crossing the English Channel and was diagnosed with stage four lung cancer about a week later, just a complete shock to our lives, our families' lives, and the community that someone so healthy, putting themselves in the best position to, you know, take care of themselves, gets diagnosed

with such a rare, aggressive cancer, that the doctors we first were in contact with had nothing, you know, knew nothing about. And luckily for us, we were put into contact—talked with the best of the best out at Dana Farber, who have been studying this cancer to put us in the best position possible. But at the same time, there's no clinical trials. There's one clinical trial that we were put on. There's no definitive treatment plan for patients that have NUT carcinoma. And not only was the diagnosis itself so disheartening, but to hear that there's nothing they can do at the same time is, if not, more disheartening to hear for someone that you love so much.

Kristen Dahlgren 05:27

And I imagine for you, when you hear about us maybe having some of the science and the technology and the researchers knowing some of how they can get better care to patients, and yet the system, or you know that there are roadblocks in it that must be hard for you to hear. And what was your experience in kind of—trying to get the best care?

Speaker 2 05:53

Yeah, I think we were lucky to have a lot of connections to the best of the best, like I said previously, but at the same time, when you meet researchers who are dedicating their lives to putting people in the best position to live another day, I think that gives you hope, and it gives you the opportunity to pour your heart. Ever since I've lost him, I've been wanting to do everything that I can, to learn as much as I can, so that families who are diagnosed, because we know it's going to happen, that they have the best care lined up for them, and being a part of the NUT Carcinoma Alliance, I'm banding together with other families who have been afflicted by this cancer, and meeting people here who have also been diagnosed with rare cancers, rare disorders, rare diseases, that are collaborating and coming together for their disease-specific needs, and it's been really inspiring to learn more.

Kristen Dahlgren 06:45

Yeah, and I want to stay on that for just one second, because you've talked about how rare cancers, when banded together, aren't actually that rare. What are you working towards in that?

Maddie Musselman Woepse 06:55

Yeah, it's been interesting, because I think when your diagnosis is given to you, you feel in isolation, and I have met so many people that it's proven to me that there's actually hundreds and thousands of people living with rare cancer, rare diseases, rare disorders. And I think that collaboration fits perfectly in being able to push the needle forward. That research needs to be done, funding needs to be given to this area of rare cancer, rare disease, and you don't know if it's going to happen to you, and when it does, it's again, it's "What can I do now to make a difference so that more people aren't losing the ones they love", and

meeting special people like this, I think is a great starting point. I'm just in this space for the past year. It's been very healing for me being a widow now and stepping into this space and trying to turn it for good.

Kristen Dahlgren 07:44

And Jesse, I know you share some of that urgency in trying to get better treatments to patients as quickly as possible. What are you excited about in this moment?

Jesse Boehm 07:58

I'm not an Olympic athlete, I won't mention, but I did pass my MIT swimming test by spending three minutes treading water in the pool when I was an undergraduate. So I'm very intimidated sitting next to Maddie. I'm most excited about team science in this moment. This is a super challenging moment for cancer researchers in the academic space, in the philanthropy space, and in the industry space, but there's this incredible moment of urgency to come together to tackle really big problems, like the one Maddie is describing, by harnessing the power of collective, team-oriented science. And that's a big part of what we're trying to do at Break Through Cancer. I'm the chief science officer of this new organization. We're a funder that tries to bring catalytic teams together to tackle translational problems in common cancers and in rare cancers, to do new things with small, nimble, early trials, with very deep science that are difficult to do otherwise. But in addition to being a funder and a foundation, we try to be a catalyst of actually enabling professional management, professional data engineering, software engineering, data sharing and exchange so that every young scientist and a few old scientists have everything that they need to work together as part of a team. And we think this is a very new model of how you do science. We call it radical collaboration. It's not just regular collaboration, it's—it's radical collaboration. And I think if this model takes hold, it'll be useful not just to our organization, but to solve many challenges across—across the ecosystem. And I think rare cancers are a great example of where we could be helpful.

Kristen Dahlgren 09:31

And I imagine radical collaboration involves other countries. So let's move on to Ian. You oversee one of the largest cancer research portfolios in the world at Cancer Research UK. What are you seeing, and what excites you in this moment?

Iain Foulkes 09:48

Yeah, I mean, just to build on what Jesse said, actually, and what you've just introduced, Kristen, as well. So, I think one of the exciting things is this international collaboration. I think in a world where. You know, we're seeing perhaps national, you know, boundaries sort of be erected and come up. You know, I think we see our role as a philanthropic organization, as a foundation, to bring the very best minds together, regardless of nationality, regardless of border. You know, like Jesse, we really sort of celebrate that whole

opportunity. We have what we call our Cancer Grand Challenge program, where we sort of outline what we think are the critical questions in cancer research, we provide the funding that allows the very best teams around the world to come together, and that's sort of really led to some extraordinary science and extraordinary research that, you know, wouldn't really be there otherwise, because most funders in country fund in country. So I think that's a really important thing, but we're seeing some really exciting things. I think, you know, we talk a lot about treatment, but I think from our perspective as well, if we're really going to beat cancer, we have to get the prevention and early detection sorted out as well. It's a very complex disease. We know with treatments that, you know, resistance can occur quite early. We're seeing a lot of really exciting areas in prevention, both in terms of stratifying risk, personalizing risks, we really understand what sort of risk profile we might have. And to Julian's point, you know the concept of bringing in vaccines, not just for HPV, but also for high risk groups, perhaps, you know, lung cancer, smokers, this sort of thing. And that's tantalizingly close. I think it's a really new wave of innovation that's going to come through in that space, and then it lead into it more early detection as well.

Kristen Dahlgren 11:25

That's always the interesting thing for me, too. In these conversations come up, do we focus more on the early detection and the prevention? Do we focus more on the therapeutics? Obviously, it needs to be both. And you mentioned liquid biopsy earlier. I know, in my experience as a patient, I'm five years out post treatment, six years from my diagnosis, and I'm not getting any liquid biopsy blood tests, because my doctors say we don't know what to do with it. We don't have the intervention. So my course of treatment is to wait, and when I get a headache, they'll scan it, or backache, God forbid, or, you know, and so, you know, you mentioned that technology. How important is it to have that two pronged approach? Of like, we need an intervention or something to do once you're diagnosed.

Julian Adams 12:18

It's critical. It's not really helpful to a patient to tell them we think you have cancer, or we confirm that you have cancer, and to do nothing about it. So number one, why the liquid biopsy specifically? And I'll give an example, and this will be a project that I'll describe —by the way I do collaborate within that foundation, we welcome you as well. Low-dose CT is an FDA-approved standard for smokers with lung cancer. It has 1 percent utilization on any given age 50 and above, and the problem there is that people just don't come back for their annual checkup. It's not like a mammogram, it's not like a colonoscopy or other modalities. So we picked this particular case study that if this is failing, meaning there's no adoption, we're going to do multimodal liquid biopsies, which means blood, saliva, urine, excretion in general, and look at multimodal approaches, of course, cell-free DNA, of course, proteomics, metabolomics. Actually, for lung, there's volatile organics as well, and eventually, nobody said the word AI yet. So I might as well start. If you take all these analytes and have a limit of detection, which is the big problem in detecting cancer, if you ask the algorithm to find the multimodal approaches, it will do a better job mathematically of finding the most sensitive, because the key is sensitivity and specificity, so that it's a reliable test before that one is even necessarily symptomatic. So that's one component of this. And then, of course, you have to intercept it. So that's what drew me to the vaccines, but other modalities of treatment. There are, of course, plenty of good drugs. Surgery is a great option, by the way, if you're stage one disease, if you can detect stage one

disease, you have a 90 percent five-year survival outcome, with many of those patients actually cured. If you're stage four disease, your five-year outcome for most diseases, on average, is about 10 perecent not only that, it's seven times more expensive to treat stage four disease than stage one disease. So all of the signals tell us work on early detection, but we need also the interception component. And that's where all the other innovation comes in to include other modalities—not—including immunotherapy, etc, etc. And vaccines are an immuno—immunotherapy.

Kristen Dahlgren 15:11

Yeah, as you say, I'm going to say yes and—or yes, but on the surgery thing, yeah, a great—you know, I'm alive thanks to surgery. It's not always easy, and so, you know, taking quality of life into account for some of these major surgeries, like mastectomy, I dream of a day where we do have the less toxic, less damaging things that don't leave you scarred in many ways for life.

Jesse Boehm 15:39

Kristen, can I add on one comment to the early detection conversation? I'm a bit on the fence about whether early detection, for the sake of early detection, will be an unambiguously a good thing. Clearly, we want to find bad things early and we want to be able to intercept, but many of the things that we're finding early will not go on to harm patients, if we don't deploy the tests appropriately. Each of us has in our pancreas lots and lots of KRAS mutations and growths, and almost all of us won't go on to develop a pancreatic cancer. I think the biggest opportunity for detection interception is in the minimal residual disease state. This is, of course, when the tumor has been surgically removed and often treated. Five to ten years go by, a tumor comes back, even though it may have been below the limit of detection on a radiologic scan. So we know there's a few cells, maybe tens or hundreds, left over. But many of our technologies, up until now, haven't had the sensitivity to find and track and monitor. I think what gives me a lot of excitement and hope is similar to what Julian said, the ability to sequence and create a personalized blood biopsy technology for the mutations or the breakpoints that are in that particular tumor, to be temporally monitored, in that MRD state. And because, you know, the patient has cancer, you know you want to intercept based on the molecular biology of that tumor, if you can track it. And some of the new therapies, which are now matched in a precision sort of way to those molecular profiles, could now be moved into MRD clinical trials. And that's the thrust of about $30 or $40 million of our efforts thus far.

Kristen Dahlgren 17:25

And Maddie, you were, you know, we were talking a little bit backstage, and you were educating me about NUT carcinoma. And Patrick was healthy and young and wouldn't necessarily have fallen into a screening program, but it's something you've thought about a lot, because this does predominantly affect young people. Where have you landed on how we maybe could make things better and diagnose this earlier?

Maddie Musselman Woepse 17:48

Yeah, I think you know, for us, we found out almost accidentally, he had a cough and got an x-ray, and it was a little cloudy, and that kind of started the whole process of his diagnosis. And luckily for us, we went to, and it kind of blows my mind, actually, he was at a local hospital, Hoag Hospital, in Orange County, where he got a biopsy done and they stained him for NUT carcinoma, which, when we went off to, you know, City of Hope, UCLA, gave them our slides. They didn't know what that cancer was. And, you know, considered top, you know, top places in the world to be treated. And you know, you just meet with a doctor and they can't help you. I think it's surprising that, you know, a place that small diagnoses you, and then you go to these big, big facilities and they're unable to treat you. And you know, we traveled to Dana Farber, and you meet researchers that are dedicating their lives to it. And so for me, I always thought, well, I'm like, how did some place so small screen us and find out about this? How can we make sure that facilities across the US, across the world, are screening and testing young adults for cancer, people who are living with chronic diseases? And you know, for our generation, a lot of people are talking about health. How can we live healthy lives? We're working out. We're exercising, especially coming from an Olympic background. How do we make sure young adults, kids aren't getting cancer, and how do you screen them for it in early stages of their life? Because again, it kind of blindsided us, thinking that we were doing what we needed to to not get sick.

Kristen Dahlgren 19:17

And you were getting what's current standard of care.

Maddie Musselman Woepse 19:20

Exactly.

Kristen Dahlgren 19:21

And screening everybody.

Maddie Musselman Woepse 19:23

Yes.

Kristen Dahlgren 19:23

Is something that's not financially possible or feasible. I'm wondering, Iain, though, if this is someplace where AI might make a difference.

Iain Foulkes 19:34

Yeah. I mean, I think there's a lot of froth about AI, as we all know, but there's some real substance to it as well. I think there's a real sense that it's really going to accelerate our work in this space. One of our institutes in London, the Francis Crick Institute, is located right next door to DeepMind, which is where DeepMind was founded. Google DeepMind, they've applied this whole sort of AI technology, obviously, to one of the biggest problems in in biology, which is how proteins are folded, which is a really critical sort of step we need to understand if we're going to design better drugs and so forth. And they took a whole, you know, 50-year data set of incredible science, and applied their algorithms to that, and they can now predict. So AI's done something humans couldn't, which was, you know, infer structure from these—from this data. And I think that's where AI is really going to help with cancer. And cancer biology is an incredibly data-rich area. You know, we have a ton of data across all the scales, from, you know, single molecules to cells, to tissues, to organs—to that—to the to the whole patient. And we, as humans, are not going to be able to assimilate all of that and infer things from it. We've got a program actually looking at drug combinations. And this is, again, I think, an area where AI can really help. There are about 2000 drugs FDA-approved in use today in oncology. If you were to think about, you know, how can we apply drug combinations to a particular cancer, drug A and drug B, the maths on that suggest there are 2 million different combinations. Now you can put a filter across that and say, actually, if you got rid of the duplication and things like that, you could probably get down to 25,000 combinations. That's a lot of trials to do. That's 50 percent more trials in the world today. AI can really, sort of help us put together much more rational approaches to how we might combine drugs and so forth to attack a particular cancer. And I think we're going to see lots of advances in that pretty quickly. We've got a number of programs and that space we're really excited about.

Kristen Dahlgren 21:42

I use the UK a lot as an example of, look what they're doing there. I mean, in cancer vaccines, they're giving out 10,000 as part of this national program to have more robust clinical trials. Lennard Lee and his team at Ellison Institute of Technology are using the super computer and have been given access—I don't know—Jesse, does it? Does it feel like other countries are doing things better now? Are there things we can learn from that? I think the collaborations which we'll get to see where you're working with them—

Jesse Boehm 22:13

Kristen, that's where I was going to go. I think each country has unique strengths and perhaps some vulnerabilities, this incredible capacity in Europe, in the UK, obviously the National Health System provides opportunities that in the US we don't have. But there are also different types of experiments happening in the United States that are, that are quite exciting as well, and that's why, when we think about collaboration, either of the radical variety of the regular variety we have to we have to think about going across international boundaries. I think a particular space that I think both Maddie and Iain touched on a bit is in the application of of AI. But a challenge is that I think rare cancer genotypes and rare cancers themselves probably won't benefit from these AI technologies unless the data sets that we generate as an

international community power the algorithms to be adequately ready to predict, and that's something that's hard to do one institution at a time. It's hard to do one one country at a time. So I think there is an opportunity to unify across the globe for some of the cancer types that are that are understudied. And if we don't do that now—the session is called "closing gaps"—if we don't do that now, we're going to be here next year and the year after lamenting, I think, the rare cancer gap as AI rolls out.

Kristen Dahlgren 23:28

Absolutely. Julian, do you want to either add to that or tell us more about your collaboration?

Julian Adams 23:33

So, I would just make a pitch for—for the for vaccines and where to use them. I agree totally with Jesse. It's in the MRD state where we're going to prove that the vaccines work. If they work there, then they'll work in prevention, even if you have a KRAS mutation and are never going to get pancreatic cancer. A vaccine is about the safest treatment you can get. And I'm going to talk about one platform, if I may, pitching vaccine. So

Kristen Dahlgren 24:03

I'm all in, keep going.

Julian Adams 24:04

I'm collaborating with Michael Fishbach at a University, Stanford. He has made a major discovery, that if it bears fruit, and we're going to fund it, he has discovered that there are commensal bacteria that live on our skin, specifically staph epidermidis. We don't know why it's there. It colonizes all humans. And what he's done in the lab, of course, and in mice, is he took a melanoma antigen, transfected it into a bacteria, grew up the bacteria, and was able to cure mice of melanoma. Initially, prevention, of course—and it works, but eventually the tumor itself and combined it with checkpoint inhibitors, but he was able to cure mice with this. What's the advantage of this? Bacteria can be grown in 100,000 liter vessels. The application is needle-free. He took a Q-tip and swabbed the forehead of the mouse. For humans, it would be probably a nasal swab, and if the bacteria colonizes, he was able to show, and has been able to show and published that the antigens actually go to the draining lymph nodes, so you can create immunity, actually. And so what I'm excited about is like, let's work on the professional antigens we've mentioned, KRAS, P53, you take care of those two antigens that are, you've got 80 percent of cancer, solid tumors covered. We're not ready for prevention studies, because they would take millions of patients and probably 10 to 15 years of follow up. There are certain medical systems in countries that could do that, certainly not in the US, I think. But the MRD status is where we're going to prove ourselves with gentle treatments that will prove the point, and then they could be broadened. I should mention, the NCI has done a lot of great work, of

course, over the years, they're 7.2 million a—billion dollar budget, only 9 pecent goes to prevention and early-stage treatment. So we've, kind of systemically got it upside down by necessity, because obviously a patient with symptomatic and advanced disease has to be treated immediately, but a patient who's going to develop a disease, I mean, we need to understand and bridge that gap and the whole continuum of cancer susceptibility to actual development of cancer, and then progression of cancer. So it's all important, but we have to sort of balance out what we can do in 2025 and beyond. So I think there's a movement coming around that these are actually tractable problems that can be solved.

Kristen Dahlgren 27:07

Right. So let's build on that a little bit. And this is sort of where my mind goes every day. I started this with the idea, knowing that vaccines are not a monotherapy, and there's a lot of other things, like, what if we put the same value on lives that we did during COVID. Can we—do say we're say—let's take money out of the equation. We know that funding is an issue, and it's a big one, but let's build on Operation Warp Speed for cancer. Jesse, what would what—you're in charge of it—where would you go with that? Who would be at the table, and where would some of the focus be to get it done quickly with as big an impact as possible?

Jesse Boehm 27:53

Kristen, I think that's the right way of framing the question. I think about 1600 individuals die every day of cancer in the United States, it's the same number of people that died every day at the peak of the pandemic, when all of us put everything aside and decided to work together across institutional boundaries, to do absolutely everything we could to solve the problem. And there should be no less urgency around cancer. I think the solution is to build new structures and incentives to allow for that urgency to not just be, you know, something we say, but something that actually produces real, real outcomes. I think one area involves organizing around fast, nimble, early trials, inviting patients to participate in phase zero, phase one, 10- to 20-patient cohort trials in which new therapies are tested, both immunotherapies and regular therapies, in willing patients, so that we can learn as much as possible from each patient's experience with a particular therapy, and to use those—then—patient samples to come back to the lab. Genomic technologies, single cell technologies, TCR, BCR profiling, etc, to definitively learn how that therapy is working in the human patient. Clearly, the NCI and the NIH are moving away from murine studies and emphasizing human and other types of studies. And I think we've often been, you know, quite paternalistic and maternalistic to say, "No, we—you know, patients aren't interested in that type of trial". We shouldn't. We should spend another 10 or 20 years more patients dying, of course, before we invite them to participate. But I think in many communities, we've had this experience in glioblastoma. It's now safe to test a therapy in the human brain and take multiple repeat biopsies after the therapy is administered without undue bleeds or harm to the patient, to actually assess the brain tumor, glioblastoma, as it's responding to therapy, as well as blood and CSF sampling, and in real time, get longitudinal brain samples to teach us how therapy is working. We've enrolled about 11 patients on a trial, more patients want to participate in this type of experiment than we ever imagined. 330 biopsies from 11 patients, and you can just see temporal dynamics of how the GBM tumor is responding to a therapy that you would never have been able to see in a dish or in a model. So it's a small microcosm of, I think, a larger

construct that could roll out across diseases, keeping really patients and families really at the center of a learning system of the future.

Kristen Dahlgren 30:27

Right, and when we're talking about GBM or pancreatic cancer, and seeing incredible results in some of those studies, I mean, that's new. That's groundbreaking, life-changing for people with those diagnoses.

Julian Adams 30:39

Can I say something a little bit about "warp speed," because I think—it's a—it's an apples and oranges comparison. For COVID and infectious disease, we had the target. It was just a question of scaling and developing the multiple technologies, notably mRNA vaccines. But it was one—it was the spike protein that led to the breakthrough. We have to remember the cancers, hundreds of diseases, including these very rare diseases that you spoke about. And I don't think warp speed is the right terminology here. I think we have to enable the technologies to get to the place of warp speed. So for example, just even in vaccines, can we use off-the-shelf vaccines? Then we can scale, if we can use that commensal bacteria approach? Yeah, we can do a billion doses, 5 billion doses, no problem, and it'll be a penny a dose. So we that will be a warp speed project. But what if it doesn't work? Then we have to go back and then personalize it. Personalized treatment is not warp speed. Personalized treatment requires a completely different type of infrastructure. So there are other modalities that I'm excited about, and I want to talk about theranostics for a moment.

Kristen Dahlgren 32:06

Sure.

Julian Adams 32:07

So theranostics, for those who don't know, it's diagnostics and therapeutics in the form of radiotherapy treatment, but it's using radionuclides that can transmit energy coupled to a homing antibody or a homing peptide protein that can find the cancer. So first, you detect the cancer with great sensitivity using these very, very sensitive techniques, and then you can blast those tumors with either beta energy, beta radiation, or I'm really enamored with this alpha radiation. Alpha radiation is basically the helium—helium nucleus, which is short path length. There are no—there's not a lot of tissue damage other than the tumor you're targeting. So getting to kind of—the kind of selectivity where you could really just hit the tumor in question, we already have our first—PLUVICTO and a few other drugs have already shown that using these radioisotopes can be very useful. We're just seeing the beginnings of this, and again, a whole new area of whole new modality of treatment. This is also to be combined with immunotherapy. The plasticity of cancer. As cancer evolves, it mutates, and you have—new mutate—you have new challenges all along.

The only system, organ system that can work with the plasticity of cancer is the immune system, which is also a plastic and evolving system. So the immune system can watch the cancer evolve and the immune system can evolve. We just have to help it. So we need these immunotherapies, which were, of course, the discoveries of this century, and are now in common use—in use.

Kristen Dahlgren 34:10

So obviously, there's a lot of technologies that are that are there and deserve trials and developments. My point in warp speed was, how do we get these two patients as quickly as possible. And so what are, then, some of the roadblocks, pain points, bottlenecks.

Julian Adams 34:29

So they're being addressed. I think Jesse's pointing out, you know, doing these early phase, zero phase, one trials in kind of window studies before you have to go to the armamentarium of standard treatment just to get a signal. So that's very helpful, because if you take heavily pretreated patients, you may miss that signal for a very promising treatment. So—and we are working with regulators, the FDA—and I, I heard Marty Makary speak this morning. They're open to these ideas. So the FDA is evolving as well as we are evolving. They are not our enemies by—you know, they're, of course, they're our regulators, but they want to work with us as scientists to develop the promising technologies. So I think there's educational crosstalk from the drug innovators all the way to the regulators, and we're going to find pathways forward, the n=1 patient, the serial biopsies that Jesse described in in glioblastoma. How else are you going to study it? The front line treatment is toxic: chemotherapy and surgery. What's left behind is very little to work with, because you now have a you have a death sentence, essentially. So we do need these window trials to be able to execute on these ideas, and then maybe eventually they do turn into warp speed. The NUT carcinoma could be sequenced, we could make mRNA vaccines. We could do these things, but we need cohorts of patients to be able to do that. And I hope we can treat all cancers. We've done something in rare sarcomas, etc., in a similar fashion. So we—we like to promote these rarest of cancers, and we have innovation summits. We're actually collaborating with CRUK in January to put a bunch of these innovation summits together to see, can we treat GBM? Can we learn how to treat childhood cancers? Can we—what about early onset cancers now that we're seeing younger patients, age 30, getting colon cancer, which we've never seen before.

Kristen Dahlgren 36:52

Right. And to your point, I mean, I think earlier this year, I heard a lot of panic in researchers, you know, as they were trying to figure out what was happening, where the funding was going, if it was being cut, what this administration, what regulators would do, and just where we would come out of this. And I think we're still waiting to see exactly what that looks like. But what if we saw it as an opportunity to rebuild a system that hadn't gotten us there yet? What would that look like? And, you know, I know, Iain, you're from the UK, so put on your American hat for a moment. And, you know, as a world, how do we, you know, how do we build something that can get these big, bold things across the finish line as quickly as possible?

Iain Foulkes 37:41

Yeah, I mean, I think it's got to—again, it's got to come back down to collaboration. I would put in a word for you know, we lose that fundamental science, and that's that's gone, and it's a huge problem. You know, right now we talk about warp speed. We have a huge attrition rate on the drugs that are coming through the pipeline, and often they're failing because we don't understand enough about the biology. You know—you've talked about—we're all walking around with these driver mutations. The average six-year-old has 100 million mutations in these important genes. We don't understand enough about the biology. And, you know, all of that funding is critical, and we, you know, we lose that at our peril, I would say, so that's, that's a vital piece, I think, from our point of view. You know, there's a huge amount of data in the world. This is where I think AI can really help us. We talk about collaboration. We need to do the research together, but actually, how we can solve that problem of integrating our data sets across borders, how we can ensure that we've got the, you know, the sort of patient will the consent in place to sort of solve some of those problems, because there's, there's so many answers out there already that we just aren't, you know, providing access to and I think if we can lower the activation energy for how scientists can work across those borders, that's going to be a really sort of vital thing. And I think AI can provide some of the tools for that—we don't need—don't need to lift data. You know, scientists can do that virtually. Can go where the data is. A lot of that's been solved. And I think we can learn from other disciplines. You know, the physics community is a much more collaborative community than the biology one. So there are definitely things we can learn from others, I think.

Kristen Dahlgren 39:19

That was the first thing when I started having these conversations about the science and what was available, I said, "Well, what's holding it up"? And it was scientists are working in silos. And I don't think it was a deliberate thing. What I've noticed since there is sometimes nonprofits and patient advocacy groups are also working in silos. You know, there's a limited pool of resources—

Julian Adams 39:39

Except for us, yeah, we're working together, right?

Kristen Dahlgren 39:42

And we'll all partner after this as well. Somebody had the same question that I was going to move on to too. It's about equitable access. So, I don't know who wants to take this one, but how do we ensure that there is equitable access? Access, that we're meeting patients, maybe where they are, that these that these trials are available to people, so that we're getting a good cross section.

Jesse Boehm 40:12

I think there's a few different ways of answering your question, Kristin. In the GBM example, the ability to sample a tumor many times over is not something that is equitably accessible to everyone around the country or around the world because of the need to be at a major medical center. I think this is a place where liquid biopsy, as a surrogate for the deep brain sampling, either through plasma or CSF, could be tremendously democratizing. And I think blood biopsy writ large, even while not quite at the price point yet, or the sensitivity threshold yet for most of the questions we have, ultimately will be quite democratizing. I think, on the discovery side, to Iain's point, we have to make sure that the data that's collected is appropriately diverse from ancestry, ethnicity, socioeconomic perspective, so that there aren't hidden biases upstream. Every time we look at a computational algorithm developed in the post-TCGA era, we find hidden sources of biases about how reads are mapped to HG-19 or HG-38 you know, the genomes that were actually quite Eurocentric at the time. There are new tools to solve that from a computational perspective, and then we have to make sure that as patients enroll in these trials, whether they're small, nimble trials or large trials, that any inclusion or exclusion criteria that are crafted around who gets to be in those trials are appropriate. We've kind of done a retrospective analysis at Break Through Cancer, and realized that actually many trial criteria are simply just copy and paste. The clinician just keeps copying and pasting whatever criteria they've been using for the last 10 years, even when those criteria have been abandoned by major communities. So there's many things that can be done, and I think we need to share best practices together.

Iain Foulkes 41:44

I think we have to also go where the patients are, which is what you said, Kristen. So we can talk about, you know, the Grail study in the UK. It's a big early detection test in multi-cancer early detection test in the NHS, but they got to 140,000 patients in less than two years, or participants, rather, not patients at this point. But what they did, very successfully, was recruit an incredibly diverse set of people. And they did that by, you know, fairly prosaic approaches of sending buses out to, you know, your recruitment—Walmart, Tesco, car parks, or, you know, around the country. And really went into communities. Really worked hard with those communities to get over some of the issues, the preconceptions that people might have about medical research and so forth, and work really hard on that, and have got an incredibly diverse set of patients as a result of that. And I think we've got to work harder to get out there as scientists in the community, explain the work that we're doing, build that trust. And I think we'll—that would benefit those issues.

Kristen Dahlgren 42:58

And I like the Cancer Vaccine Launch Pad model too, as Lennard explained it to me, is, you know, the community hospitals are referring to the larger hospitals. I feel a lot of times like our community and more rural hospitals are not getting or don't have the awareness of where they can be sending patients, and then patients affording and being able to get there—you were going to say something.

Julian Adams 43:17

So there's a couple of things that we have done extraordinary work. I mean, I lived through the HIV crisis and discovered one of the HIV drugs, and we transformed this disease from a death sentence to a chronic treatment. We got no credit for it, actually. The COVID pandemic. We solved this as a community, as a global community, multiple countries were involved, and again, have got no credit, and scientists have not done a great job of communicating their successes and—and, therefore, there's now the greatest credibility gap we've seen in our lifetime, and what we are not very good at is telling those stories. The storytelling component actually reaches the public. If you can't tell the story, we become the liberal elite, and then we become—we are alienating half the population, and there have been lots of surveys on this. For example, if you ask the public, do you believe the public taxpayer dollars should be used to fund research? The answer is 60 percent say no, but if you ask them about cancer research, it's a 90 percent say yes. So it's how are we asking these questions, and how are we presenting ourselves to our fellow citizens and colleagues? I think, Stand Up to Cancer, spends a lot of time of thinking about the storytelling and telling all stories, from the rarest to the—of diseases to the to the big problems, we don't—I think if you polled people. The peak of cancer cell death was 1993 we have 34 percent fewer deaths in 2025. That's 5 million lives saved. Who knows that? These statistics? Now, again, people don't remember statistics. So how do you say in three words, "Yes, we can"? Or how do you say in four words, "make America great again"—again. I'm trying to de-politicize this as much as I can, because if you can come up with tag lines and —but just reach the reach the public so we can work together, because the enemy is the disease, not—the enemy is cancer. It's not political parties, it's not even other countries. We haven't used the word China yet. China, if we don't do it, China is going to do it. They have the 100-year plan. They don't change administrations every four to eight years. So if we don't do it, it'll go somewhere else. And if our industries don't thrive in the US or the UK or anywhere else, they'll go to wherever they need to thrive, because eventually we are in a for-profit system, like it or not, it's part of our economy. With $5 trillion spent from our GDP on health care, that's a big—that's a big sum. So we have to put the whole system together, and the it's incumbent on the scientists to tell—to do better storytelling, and that's what we've adopted at Stand Up.

Kristen Dahlgren 47:05

And let's talk about that messaging, and please do scan and send us some questions if you want some asked. Say, a cancer vaccine does become a reality. What can we be doing now to make sure they're accessible and make them something that people trust and want to take? You know—we've thought about changing the name of our organization from Cancer Vaccine Coalition, because people misunderstand—that this is not necessarily a preventative measure, but a therapeutic, or to prevent recurrence at this point. And, you know, there is this discussion over other types of vaccination in this country that it does get caught up in. So I think communication in that instance, and what we're trying to work on now, we're making a documentary, and we're, you know, we're working on that messaging, because these are things that will be used in patients who are being asked to put toxic chemotherapy, mustard gas, in some cases, into their veins. It's not a question. I have people every day, when can I get it? Where can I get it? How can I sign up for trials? So, in your cancer populations, there's not an issue or a debate. How do we message to the general public of this moment that we're in and what's possible if we just lean into it? Jesse, do you think about that a lot, or?

Jesse Boehm 48:32

I think we have to be cognizant of the complexity and of the pressure points. But as you were signaling, Kristen, I think it's a really important to message, the hope and the optimism. This is the most, I think, unique moment in the history of this disease. We have therapeutics, small molecules. There was just a Washington Post story about these new KRAS, drugs and pancreatic cancer. I mean, gosh, we're targeting KRAS now. It's going to be FDA-approved quite soon, and this is going to be the next wave of BRAF, EGFR, like drugs, and we're just gonna look back and say, "Well, of course, we could always target KRAS". That's just gonna be transformative for lethal diseases. Same with cancer vaccine, same with Car-Ts. These are amazing, amazing therapies. And when an individual, I'm sure, Maddie, has even more perspective on this, but when individuals get diagnosed and they consume the literature, they often hone in on these breakthroughs. They want a cancer vaccine representing their tumor. They want a therapy match to their tumor, and with a bit of digestion of kind of where we are as a field, then there's the ability to try to navigate the system. We just have to make sure that the system is then ready to deliver the promised benefits. And that's really where data generation and data collection comes in. We can't just say cancer vaccines are great, or Car-Ts are great, or this is great, or that, or we have to build the evidentiary base to be able to look that patient in the eye and say, you know, we've treated 100 patients just like you, and 70 respond and 30 don't respond. And this is the data and here's the evidence behind that. And so we have to temper the enthusiasm that is at this moment, but we also have to lean into it and communicate it quite, quite clearly.

Maddie Musselman Woepse 50:10

And I have a small comment on that kind of in terms of, like, a patient advocacy standpoint, of like, bridging the gap and creating a bridge from patients to what you guys are doing. I mean, brings me a lot of hope, just like listening to what you guys are working in and how can we get rare cancers—for us, it's like I will literally do anything. I will give you all my slides. I will give you literally my body to save my life. And so, from my husband's point of view, it was like we were willing to do anything and everything and to only be put on one trial, and that's the only option. And now that I'm standing in a position of, you know, future patients coming to us as an alliance of, hey, you know, we've lost family members, but this is where we can now send you to get care. And it's just exciting to hear the options, because I think that opens the horizons for rare cancer to be considered and raising awareness. On my part of you know, there is work being done, and how can we get it into your hands of, you know, patients? Yes, it's rare. There's not that many, but maybe, if we screen more, maybe there'll be more patients that we don't know about. And then also, just, how can we help you, like as a patient advocate, giving you what you need from these patients that they're doing their job. They just need to focus on healing, being given what they need to be given. And now that I'm in my position, I want to give you guys what you can to study something that is now really near and dear to my heart after losing someone from it, and I'm just excited to be in this room hearing about what you guys are doing, because now I just want to give you all the registries of NUT carcinoma to go fix it.

Kristen Dahlgren 51:41

We have a phlebotomist backstage.

Jesse Boehm 51:42

We have to be able to tell these stories clearly and consistently. There's a simple way to prevent 80 percent of advanced ovarian cancers. Ovarian cancers of the serous variety, come from fallopian tubes, not from ovaries. And if a woman elects at a time of tubal ligation, when fertility period is done to have tubes removed, instead of a tubal ligation, there's an 80 percent reduction in risk over one's lifetime in developing serious ovarian cancer. A British Columbia study just proved it. We're trying to broadcast this with the American Cancer Society's National Health Movement. When people hear about that, they say, "No one ever told me that". And then everyone texts or calls someone they know in their family and say, "Gosh, I'd like, I'd like to have my tubes out", you know. So these types of stories, these simple messages, when there are clear and effective medicines, I think the KRAS drugs will be another example. I think those give us hope, and we have to make sure we're communicating them, them clearly when they are an option for patients.

Iain Foulkes 52:46

I think we have, with the with the HPV vaccine as well. I mean, we've got to a point now where science will, in a generation, eradicate cervical cancer pretty much, you know, and it's incredibly powerful story. And I think we have to use patients to tell those stories. I think, you know, patients have families. They have mothers.

Kristen Dahlgren 53:04

I was gonna say, Maddie, it's so important what you're doing and speaking out, which isn't easy, especially when you've lost someone. I think is such an important part of this. And someone had also asked, "How do we integrate patients and caregivers into the creation, into trial design". Are there ways that maybe you wish you and Patrick had been asked more or could have participated?

Maddie Musselman Woepse 53:29

Yeah, I mean, one, I think it's hard, because not everyone wants to be a part of that. I think, you know, for my husband, I felt like, you know, he just wanted to put his head down and do what he needed, whereas, from my point of view, I was researching everything possible, reading all these articles, like, can we be considered compassionate care for something that's not for NUT carcinoma, but just to try it? And I think you're willing to put yourself out there to find the best possible treatment for your loved ones. And I think there's a lot more people that are willing to do that. And I've met families who've been afflicted by NUT carcinoma that, you know, they lost their loved ones in four to six months. I got my husband for 13 months when he was battling, like, apparently that was insane. I didn't—I didn't know it at the time how his battle was four times as long as it should have been. And what did I do that made it longer? Like, how can I help other patients do what they need to have as much time as they can with their loved ones? And now that

I'm in this position, I just want to gather the resources from all of you guys to be able to be that advocate for people who are unfortunately diagnosed. And then also, I have a science background, a little bit. And if I'm going to be taking care of people in oncology one day as a PA, I want to have the right resources as well to, you know, give them a vaccine or put them on a trial and—and be that voice for them, because I got to be the voice for my husband.

Maddie Musselman Woepse 54:47

Dana Farber.

Kristen Dahlgren 54:47

Okay, so someone did recommend it?

Maddie Musselman Woepse 54:47

Yes.

Kristen Dahlgren 54:47

Because I have a lot of people say, "Oh my gosh, I went on clinicaltrials.gov and,

Kristen Dahlgren 54:48

How did you find your trial?

Maddie Musselman Woepse 54:59

Yeah, Yeah.

Kristen Dahlgren 55:00

I couldn't find anything". I mean, I went—I had the same experience, and I was already working in this field. And for my father, I couldn't find him the intervention.

Jesse Boehm 55:09

This is a clear place where LLMs could be informative.

Kristen Dahlgren 55:13

Yeah, absolutely. I mean, I think that's, that's just an easy step.

Julian Adams 55:17

I would go one step further. The National Library of Medicine is one of the institutes of the NIH—I'll say, I don't think— something like 20 years ago, I was brought in to a think tank to talk about NIH, and Francis Collins was convening the meeting. And I asked, why do you have a national library of medicine that gets $500 million a year to host PubMed and clinicaltrials.gov? Why don't you just give it to Google? They'll probably do it for free or maybe some tax incentive, and they'll do—they'll use modern software, particularly now that we have LLMs, and these are horrible databases and difficult to use, and actually a lot of data is missing, so you can't navigate. You can't be your own navigator, and that's why we have only 7 percent of patients with a diagnosis of cancer ever even enter a clinical trial. Maybe they're doing better in the UK. I know they're doing better in the socialized medicine systems because they have no choice. They don't have access to the certain therapies, but we're just doing a terrible job of storytelling, explaining to the public what are their options. The word cancer vaccine at my—the company I chair, it occurred to us years later, after we'd published, cancer vaccines, cancer vaccines, cancer vaccines, shouldn't we just call it advanced immunotherapy? Because cancer vaccines have gotten now a taint, or the word vaccine has a taint. I said, "Well, you can't put the toothpaste back in the tube. We have to live with—with—so figure it out." Tell the story a bit better, so that it's not, you know, the scourge of, you know, it doesn't cause autism. We know that. Just keep, keep at it. If I may, one more anecdote: I had the—Sherry Lansing is the founder of Stand Up to Cancer—15 years ago, she invited me to her home. Major League Baseball are big supporters of Stand Up to Cancer and our corporate sponsors. I had all of the owners of MLB in her living room, and there was me and another physician whose name I won't mention. He was going to talk about pancreatic cancer to the baseball owners, and I was to talk about immunotherapy. He went first, and he lost the audience in 30 seconds, because he went into jargon and, like, talked about complex science that didn't register, and I saw this, I have to do the opposite of that. So what I did is I was very animated, as maybe you can tell, I'm pretty animated. And I walked up to everybody, and I said, we all have immune systems, and the cancer is just evading our immune system. So can't we just wake up our immune system and recognize the cancer and fight the cancer with our own immune systems, and we have ways to do that now. That's all I had to say. I owned the room at that point, not to give myself credit, but just to talk getting back to telling our scientific story to the right audiences. Obviously, to the National Academy of Sciences, we need to speak with great precision and great authority about what we know and what we don't know, but to the general public, we are losing the battle of scientific education, and it starts in grade school and goes all the way to the—to the community.

Kristen Dahlgren 58:59

And we just have a few minutes left. So maybe this is too big of a subject to get into: How to how to pay for it? You know, what roles do you envision employers paying and, you know, who should be funding? Kind of these early detection things. Are there ways that we can make changes there?

Jesse Boehm 59:19

Yeah, I think it's very difficult for any on the discovery side. I think it's very difficult for any one funder to organize the necessary coalitions that are needed. That's why, Kristen, the type of work you're doing is so valuable. We we have to work together. This isn't about one organization or one country. We have to pool capital. We have to pool resources, ensure that discovery efforts create data that everyone can use. And then the best drugs are made. The drugs may begin expensive, and then they'll go down, but they have to be effective, based on modern science. I just see this unbelievable opportunity to work together. That's what this panel is describing. But it's going to take more than any of us working individually. There's tremendous opportunity together.

Kristen Dahlgren 1:00:02

Communication, collaboration.

Julian Adams 1:00:04

There's one entity we haven't talked about, and that's the payers. And sadly, they're not at this meeting, and they don't have skin in this game. They charge what they charge. The contracts, particularly with Medicare A, Part A, and Part B, all the contracts are private, confidential. We don't know—they—and they contribute nothing, really nothing, to health care, because if the costs go up, they pass it on to the consumer. So we need to, maybe by law, maybe by, I don't know, some collective action, hold the payers accountable, because they're part of the funding problem. Similarly, we have to tell pharmaceutical companies in biotech, where do your employees come from? They come from academic research, who trained them? That's your pipeline. That's—those are your future researchers. Why? If you get hired at Deloitte & Touche—at Deloitte, you'll get your MBA paid for by the company. You get hired at a law firm—many law firms will pay your law school fees. Why not get the pharmaceutical industry also get involved and pay some contribution to tuition, etc, etc.

Kristen Dahlgren 1:01:31

So we have more people to invite to the follow-up collaboration meeting next year.

Julian Adams 1:01:36

We should double the size of the conference. Mike Milken, if you can afford it, please bring other parties to the table, because there are a lot of missing voices in this enterprise.

Kristen Dahlgren 1:01:47

Yeah, so reach out to us. As a patient, thank you for all the work you're doing, and thank you for your time, and hopefully, we don't have to do this too many more times.

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