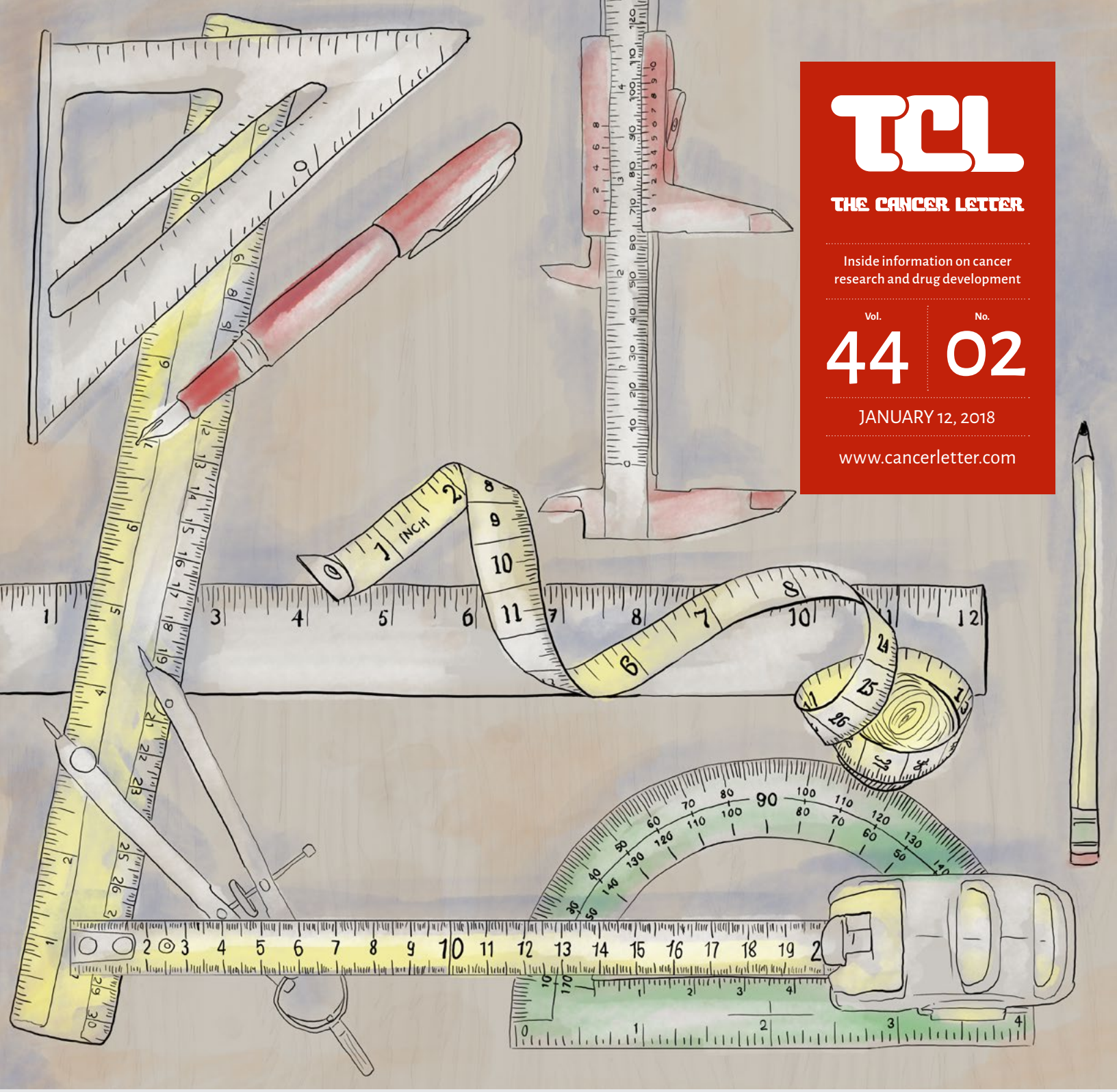

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Inside information on cancer research and drug development

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ROCHE FUNDS EFFORT BY SYAPSE TO BUILD SOFTWARE FOR MEASURING OUTCOMES IN PRECISION ONCOLOGY

By Matthew Bin Han Ong

Roche has teamed up with the precision medicine company Syapse to develop software for measuring health outcomes and economic impact of precision medicine.

The Syapse-Roche collaboration will focus on developing four specific software analytics solutions that would ultimately be added to the existing Syapse platform to generate insight and data trends.

Formed in 2010, Syapse works with health systems to integrate oncology data from electronic health records with genomic data. (The Cancer Letter, June 24, 2016).

The Syapse platform connects cancer care information across nearly 300 hospitals in 25 states—which collectively manage about one million active cancer cases, about 10 percent of cancer patients in the U.S., the company said.

Neither Syapse nor any other informatics company in oncology is able to use real-world data to provide "clinical decision support," defined as recommending treatment plans to oncologists.

Syapse, for example, currently functions as a "clinical decision resource," enabling physicians' independent clinical judgments based on aggregated patient treatment and outcomes data.

Other bioinformatics systems, including CancerLinQ, which is operated by the American Society of Clinical Oncology, are working to develop decision support capabilities. Recently, ASCO formed a collaboration with two Big Data firms—Tempus and Precision Health AI to develop commercial uses for CancerLinQ while defraying the costs of operating it (The Cancer Letter, Jan. 5).

Syapse's collaboration with Roche developed over two years with the goal of expanding Syapse's suite of interactive tools, which can be adapted to health systems and other health care providers to achieve interoperability.

The Roche-Syapse collaboration is focused on four programs:

- Developing a "learning health system" based on real-world evidence to enable clinical decision support. This could reduce the need for randomized clinical trials to demonstrate safety and efficacy of precision therapies.
- Bringing cancer care into the "value-based" era by incorporating cost factors and outcomes into clinical decisions. This is important because more expensive therapies may end up saving resources overall.
- Using patient-reported outcomes in a consistent manner across thera-

pies. This is important because patient-reported outcomes can differ wildly, depending on therapy.

- Accelerating enrollment in clinical trials by matching patients with trials. This is important, because patients treated in the community have fewer opportunities to get into clinical trials than patients treated at academic cancer centers.

Under the agreement, Roche will fund the development of these products. The size of Roche's investment was not disclosed. Roche had invested in Syapse's Series D financing, which is the fourth stage in a financing cycle for a company that hasn't gone public.

If these programs are developed, oncologists would be able to receive true clinical decision support—deriving recommendations about testing or treatment plans from the platform instead of only having access to Syapse's aggregated patient data.

Health system administrators would be able to determine, by studying both economic and patient treatment data, whether hospitals should offer new therapies based on the tradeoffs between outcomes and costs.

Patients would be able to report outcomes over the duration of their treatment and beyond—providing data on response to treatment, quality of life, adverse events, and compliance. For example, if a patient experiences severe side effects and stops following the regimen, a physician would receive a cue to intervene.

Finally, physicians would be able to direct and optimize the enrollment process to ensure that patients are accrued to the clinical trials that they have already been matched with via Syapse's platform.

"Many of these ideas have been discussed, so it's not that the idea itself is unique, it's the execution of it," Ken Tarkoff, CEO of Syapse, said to The Cancer Letter. "From our perspective, actually being able to execute on these product programs, bringing them to market, bringing the key players together, having the appropriate amount of investment and partnership to make it happen, is really the differentiation."

The collaboration does not involve selling data to Roche, said Jonathan Hirsch, president and founder of Syapse.

"When you think about typical pharma relationships and what they're trying to do, there's been a mentality where the pharma companies have traditionally focused on data access. We decided to take a different approach," Hirsch said to The Cancer Letter. "What our collaboration with Roche represents is a new type of partnership where a pharmaceutical company is coming in and saying, 'We need to go beyond the pill and provide additional value to physicians, especially with all the consolidation of oncologists from small independent practices into health system-based practices.'"

A conversation with Tarkoff and Hirsch appears on page 8.

In return for its investment, Roche would get an opportunity to play a role in developing this technology. Roche may also gain access to Syapse's network, and can develop separate studies and initiatives with the health systems Syapse serves.

"The collaboration with Syapse is a long-term partnership that will strengthen our relationship with a broad network of healthcare systems to advanced personalized healthcare in oncology," Roche officials said in a statement to The Cancer Letter. "We are aiming at combining Syapse's pioneering platform with Roche's oncology expertise and developing solutions that empower providers to practice precision medicine at scale. We hope to contribute to fully realizing the potential of precision medicine for all patients and their physicians. Our partnership with Syapse will allow Roche to do so."

This collaboration brings together groups that traditionally are unable to cooperate more fully, because of a lack of data access and transparency, said Damon Hostin, CEO of the Precision Medicine Alliance of Catholic Health Initiatives and Dignity Health. The two networks—the nation's biggest nonprofit health systems—use Syapse to integrate their cancer data (The Cancer Letter, Sept. 30, 2016).

"What really excited me about this is that there is such deep knowledge in health care economics as it relates to the use of advanced therapeutics, and we all know the cost to bear of these therapeutics," Hostin said to The Cancer Letter. "Roche is really bringing a ground level understanding of that field to the ecosystem and looking to cooperate with it.

"I was very impressed that there is a willingness to be product agnostic, meaning the collaboration is a platform for understanding and it's a window into the truth of the costs and risks, and that really hasn't been done before with these types of partners."

A conversation with Hostin appears on page 13.

The Syapse-Roche collaboration is part of an overall movement in oncology to build learning health systems, said Amy Abernethy, chief medical officer, chief scientific officer, and senior vice president of oncology at Flatiron Health, a cancer informatics company focused on aggregating data for research. Formerly, she ran the Center for Learning Health Care at Duke University.

"What we're seeing is lots of increasing activity in this space, which tells us it's an important place. What gets confusing is that we are all kind of using the

> From our perspective, actually being able to execute on these product programs, bringing them to market, bringing the key players together, having the appropriate amount of investment and partnership to make it happen, is really the differentiation.
>
> *– Ken Tarkoff*

same language around learning health systems, but it can mean different things," Abernethy said to The Cancer Letter. "The concept of a 'Learning Health System' can mean everything from improving and accelerating research to improving precision medicine, to improving the value of care delivered, to information back to doctors.

"The learning health systems language that Flatiron is using, CancerLinQ is using, that I used when I was at Duke, and that the Institute of Medicine has used—all of these things are different aspects of this overarching learning health systems philosophy.

"We're all building parts of the learning health system, and that's the reason why what Syapse is doing can be complementary to what Flatiron is doing, is because somebody needs to work on clinical decision support, and Syapse and Tempus is saying that that's what they're going to work on. Somebody needs to work on accelerating the research side of things, that's what Flatiron says we're going to work on.

"We're all working on different parts of an overall set of tasks that ultimately comes back to how do we improve lives by learning from the care of every cancer patient. You're just seeing a whole bunch of activity in this space, because I think that not only are the concepts gaining traction, but the business models around it are gaining traction. The efficiency is real. It really does lead to more efficient decision-making and hopefully better patient care."

In January 2016, Roche led Flatiron's Series C round of investment, totaling $175 million. At the same time, Roche entered into a multi-year, non-exclusive agreement with Flatiron. The companies also agreed to collaborate on accelerating clinical trials and advancing personalized medicine.

Roche said it chose Syapse because of the company's deep expertise in precision medicine.

"Their customers include some of the largest health systems and academic systems in the U.S.," Roche officials said to The Cancer Letter. "Syapse's expertise in precision medicine software and analytics solutions makes them the ideal partner for this collaboration.

"They have a comprehensive platform to scale precision oncology by integrating previously siloed patient information, providing patient-specific decision support, and matching patients to clinical trials. Syapse is also unique in enabling cancer data sharing for oncology providers to learn from real-world outcomes, which we believe is critical to moving precision medicine forward.

"The collaboration aligns with our long-standing personalized healthcare strategy of tailoring medical treatments to the individual to help prevent, diagnose and treat patients more effectively and quickly.

"As digital healthcare technologies become more sophisticated, personalized healthcare depends increasingly on integrating meaningful data from a variety of data sources and using advanced analytics to generate a complete view of patient health. Syapse is pushing the boundaries in using oncology informatics to improve care; for example, in exploring the use of real-world evidence and analytics to directly improve patient care, today.

"Combining Syapse's expertise, and its provider-driven network, with Roche's capabilities will accelerate this work and enable both companies to dramatically increase the number of people who have access to personalized healthcare."

Q & A

Tarkoff and Hirsch spoke with Matthew Ong, a reporter at The Cancer Letter.

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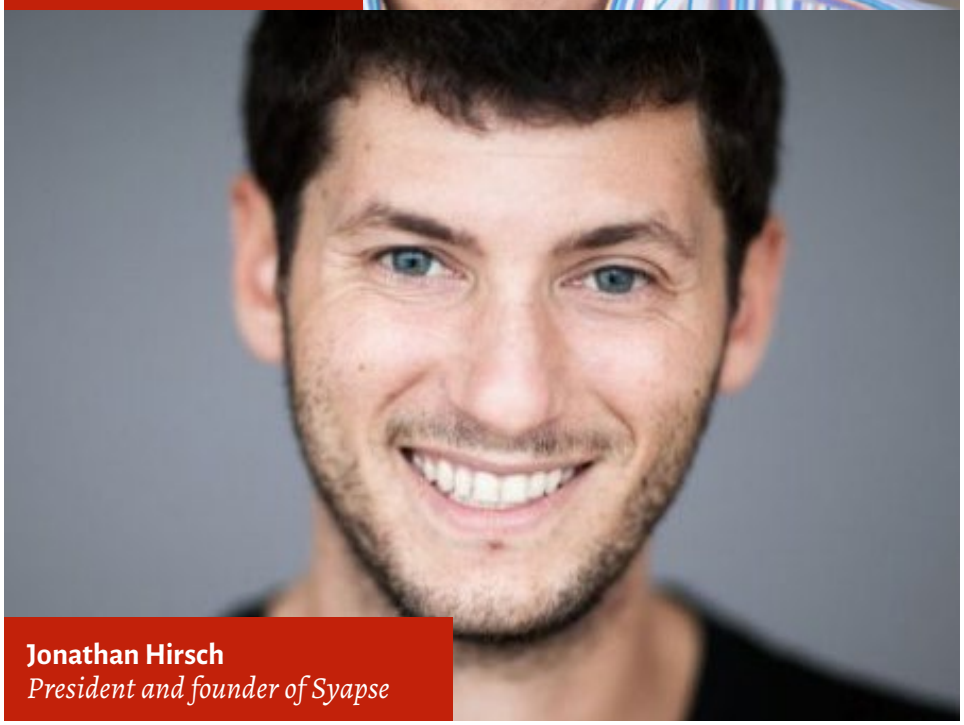
CONVERSATION WITH THE CANCER LETTER

Syapse: Roche collaboration enables us to experiment with new technology

Ken Tarkoff
CEO of Syapse



Jonathan Hirsch
President and founder of Syapse

> This represents a new type of partnership where we're working collaboratively on enhancing the experience for the physician and for the health system, and bringing in new tools that are going to help them make better decisions. So that's why we're super excited about it.

– Jonathan Hirsch

Syapse and Roche are working on building software that would allow health systems to incorporate real-world evidence into Syapse's platform in an effort to develop true clinical decision support for precision therapies.

The multi-year collaboration, announced Jan. 9, aims to develop four programs that focus on economic and outcomes measures. The programs are also expected to expand Syapse's ability to integrate patient-reported outcomes into the cancer care pathway and optimize the platform's processes for enrolling patients into clinical trials.

"Figuring out how you take all of the underlying source data and use automated methods to derive meaningful outcomes metrics is an area that's incredibly challenging in oncology right now, but more important than ever," said Jonathan Hirsch, president and founder of Syapse.

Hirsch and Ken Tarkoff, CEO of Syapse, spoke with Matthew Ong, a reporter with The Cancer Letter.

Matthew Ong: How did the collaboration come about?

Ken Tarkoff: We're very focused on continuing to develop our provider-driven network approach, where we work with large health systems to deploy precision oncology at scale. As part of that effort, we are working to bring the key players of the precision medicine ecosystem together to collaborate directly with providers.

When we announced our fundraising a couple of months ago, we added to our investor base four new strategic partners that are part of the ecosystem. Those and other companies have been increasingly interested in figuring out ways to more proactively participate in the precision medicine ecosystem.

Roche is the first company that we're working with to start bringing together the players in the ecosystem to bring new solutions to market that benefit providers and their patients.

This has been our strategy for a while. I joined as CEO 10 months ago and we started accelerating these efforts, and we're excited to announce it because it's a strong confirmation of our direction and our focus.

If you want to ask more about the nature of the relationship, this is something Jon's been working on for a while and Jon did a great job of developing it from some initial efforts into a much bigger, multi-year strategic investment.

I'd love to hear more about it. Importantly, how will this collaboration add to what Syapse is already doing and already provides?

Jonathan Hirsch: Some of the collaboration with Roche is really adding fuel to the fire and accelerating components of what we're already doing; for example, we've already been working on a learning health system network with our health provider systems. The Roche collaboration is going to dramatically accelerate our efforts, and it's going to bring their expertise to the table to help.

Many of the other pillars of the collaboration are new—for example, understanding the health outcomes and economic impact of precision medicine. That's something that we have taken some small-scale forays into in the past. Working with Roche, we're going to develop what we think will be the first-of-its-kind solution to help understand the economic and operational impact of precision medicine on patient care at a health system. This will leverage the expertise that Roche has, some of the existing technology we have, and new technology we'll jointly build. That's a new and potentially transformational effort.

The patient-reported outcomes pillar will be a new product direction for us. That's actually an idea that Roche brought to the table as something that would be very impactful on clinical care, and we're really excited to embark on this effort.

One of the things that's going to be most exciting is this focus of every strategic pillar we have with Roche, which is figuring out automated methods to derive and track outcomes measures for cancer patients.

Figuring out how you take all of the underlying source data and use automated methods to derive meaningful outcomes metrics is an area that's incredibly challenging in oncology right now, but more important than ever.

We've been doing some work on this for a little while. Roche has independently been doing some of their own artificial intelligence/machine learning work on it. So what this collaboration represents is an opportunity for us to bring these efforts together and really experiment with some new technology, see what works, and then bring that right to the oncologists that we're working with.

Forgive me if this comes across as a little too reductive, but these product programs—when they're complete, you'd basically be adding plugins and features to enhance Syapse's existing platform, right?

JH: Yes, that's really the gist of it. When you think about typical pharma relationships and what they're trying to do, there's been a mentality where the

pharma companies have traditionally focused on data access. We decided to take a different approach.

What our collaboration with Roche represents is a new type of partnership where a pharmaceutical company is coming in and saying, "We need to go beyond the pill and provide additional value to physicians, especially with all the consolidation of oncologists from small independent practices into health system-based practices."

This represents a new type of partnership where we're working collaboratively on enhancing the experience for the physician and for the health system, and bringing in new tools that are going to help them make better decisions. So that's why we're super excited about it.

Will the intellectual property for these product programs belong to both Syapse and Roche?

JH: Certain IP will be shared between Syapse and Roche, and Syapse will have the exclusive rights to commercialize the IP. We will do this in the form of products and services.

How much money is Roche contributing?

KT: That is not publicly disclosable information. What we are disclosing is this is a large, multi-year partnership.

Could you explain how each of the four product programs would impact or change cancer care?

JH: The first program, which we call Precision Medicine Insights, is our learning health network. What we're trying to accomplish there for the oncologist is enabling them not just to access all of the aggregated data from across all the providers that we work with and mine it, but to move that to the next level of providing proactive decision support using the aggregated data.

Providers will be able to derive insights about what testing or treatment to recommend for a given type of patient, and then bring that specific guidance to the point of care. The end goal is really about helping providers improve how they treat today's patients—not a research exercise for 15 years from now—but really an effort to help today's patients.

The second pillar is what we call Evidence for Precision Medicine. This pillar is more specifically targeted at the oncology service line leadership at the health system, and also at payers and integrated payer-providers. The goal is to help them understand at the population-level, the outcomes and economic impact of various precision medicine care plans so that the health system and the payer can make an intelligent decision about the trade-off between outcomes, costs, etc.

In particular, this is important right now because of all the new therapies and molecular tests that are coming out. The health system needs to be armed with the right information to understand: is precision medicine saving money? Is it costing more money? What is the tradeoff between medical and pharmacy spend? We want to help providers, payers, and pharmaceutical companies have a more informed conversation and make data-driven decisions on these topics.

For instance, health system administrators can study the economic data and decide whether a new therapy is right to offer for their patient population?

JH: Exactly. Many of the health systems that we're working with are looking at things like biosimilars; for example, they want to understand, how should that be incorporated their formulary?

The third pillar, patient-reported outcomes, is building on work that a lot of other parties have done across the industry and a recognition that actively tracking P.R.O.s and surfacing them to a physician, in and of itself, can have a positive impact (Dr. Cerami's study at ASCO last year).

As we move into the age of precision medicine, targeted therapies and immunotherapy will have different safety and adverse event profiles. It will be very important to track P.R.O.s and to bake PRO-informed decision support into clinical care. So we're going to roll out a tool to enable the clinical team to capture the P.R.O.s and to surface them at the point of care to assist with decision-making. We hope to collaborate with others who have patient-facing PRO tools.

The final one is clinical trial optimization. At Syapse we've done a lot of work on matching patients to clinical trials through software automation, and we're going to continue that. Now we're going to take the next step and look at optimizing the recruitment of the patient into the trial after the patient has been matched. It's one thing to match the patient, but we want to make sure you really optimize that process of getting the patient enrolled.

The goal there is to—and I'll use an overused word—democratize access to clinical trials. We work with a lot of very large community health systems, and our goal is to make sure that the patients in the community have access to the best therapeutic options, which, much of the time, will be in the form of a clinical trial.

For us, the clinical trial pillar is all about access; it's an access issue for the patients in the community. We're trying to work on optimizing that process. We

can do all the matching in the world but if you can't impact what happens after the match, then you really haven't helped solve the access issue.

Will these product programs set Syapse apart from what everyone else is doing?

KT: From our perspective, actually being able to execute on these product programs, bringing them to market, bringing the key players together, and having the appropriate amount of investment and partnership to make it happen, is really the differentiation. Many of these ideas have been discussed, so it's not that the idea itself is unique, it's the execution of it.

We believe strongly that building an aligned ecosystem of partners is the best, fastest, and most impactful way for the provider and ultimately for the patient to be able to realize the vision of precision medicine. We believe this increases our opportunity to deliver on the promise.

And no other company is working on building these functions and including real-world data into an integrated oncology clinical decision support platform at this point in time?

KT: I think that's right. And, a platform that is provider-oriented, driving, in particular, the health system organizations to be able to make scaled precision medicine a reality. We believe it's very important to have that platform and those partnerships together integrating and working together on that platform.

So, yes, we believe very strongly that is a differentiator and we'll have the impact on cancer care, because at the end of the day that's why we're doing it.

Q & A

Hostin spoke with Matthew Ong, a reporter at The Cancer Letter.

CONVERSATION WITH THE CANCER LETTER

Hostin: Roche-Syapse programs will increase amount and depth of risk-benefit info in precision oncology

Damon Hostin
CEO of the Precision Medicine Alliance of Catholic Health Initiatives and Dignity Health

> One of the things precision medicine really needs to do is stop being so exceptional and play by the same rules as any intervention in healthcare. This is a sign of the field maturing, where it's being beholden to any of the economic measures that any intervention would be held to.

The Roche-Syapse collaboration to develop analytics programs may enable health systems to measure the impact of precision therapies, said Damon Hostin, CEO of the Precision Medicine Alliance.

Hostin oversees the precision medicine partnership between two of the nation's largest nonprofits—Dignity Health and Catholic Health Initiatives—and is in charge of integration of oncology and other clinical data programs between the health systems. The network describes itself as the largest community-based precision medicine program in the U.S.

"As important as the core technology is, it's about bringing the ecosystem together. And Syapse has been effective in doing this on a common platform," Hostin said to The Cancer Letter. "This is, I think, a sign of the [precision medicine] field maturing, where it's being beholden to any of the economic measures that any intervention would be held to.

"Some of the benefits tend to be the amount or depth of information, the genetic markers, be it economic, and then the other dimension of it is looking at the total lifecycle or extending the episode of care so that we more fully understand the impact of the medicines or risks."

Hostin spoke to Matthew Ong, a reporter with The Cancer Letter.

Matthew Ong: What does the Roche-Syapse collaboration mean for the Precision Medicine Alliance, and for your provider partners? How would this change the way your health systems do cancer care?

Damon Hostin: In an agreement like this, just to speak generally, because in the Precision Medicine Alliance, we use the Syapse system, we of course as a major health care provider use many of Roche's products, but the agreement is more substantive that it's bringing together groups that traditionally are unable to cooperate more fully because of a lack of data access and transparency in understanding effectiveness and cost effectiveness of therapeutics in particular.

So what really excited me about this is that there is such deep knowledge in healthcare economics as it relates to the use of advanced therapeutics, and we all know the cost to bear of these therapeutics.

Roche is really bringing a ground level understanding of that field to the ecosystem and looking to cooperate with it. So, every time we hear about risk potential for, let's say, risk-based payments or anywhere in which quality is now becoming a determinant on the payer side of healthcare, Roche is actually bringing a very rare perspective to healthcare.

Now, Syapse is the platform that allows for the information to become relevant, and specifically, it is able to digitize the esoteric nature of cancer genetics, which is very difficult to put into a workable dataset alongside EMR data.

If you look at the two facets here, one of tumor biology and the other healthcare information, Syapse is able to bring back together. And I would say, the types of things that we're going to look at is, "What is the value of any given modality outside of the drug itself? What was the cost of supportive care? Did it prevent adverse events? What is the overall burden of treatment and what is the differential of different interventions there within?"

So really giving a better resolution on the natural history of a patient so that we understand the costs, the risks, and can actually do comparisons across different product types. Knowing the patient better leads to better decisions.

I was very impressed that there is a willingness to be product agnostic, meaning the collaboration is a platform for understanding and it's a window into the truth of the costs and risks, and that really hasn't been done before with these types of partners.

And you're saying this in the context of the four product programs that are going to be developed as a result of this collaboration.

DH: That's right, this is all quite formative. When you ask how is it going to change what we do, of course this is all a little bit speculative, but you know, you always say if you can get everyone to the table to get a single source of truth about what we think or what is supposed in the clinics, well, we would have a much better handle on the practice of medicine.

For the first product, the concept of the "learning health system," that is where if you're not capturing and standardizing EMR data elements and putting them alongside the deep profiling of a patient, you really can't make any conclusive findings around these populations.

What we're looking for is it isn't just the tumor profile, and it's not just the elements of the EMR, it's everything together. And so, if we're standardizing language ontologies IT systems capture, that then allows us in a much more cohesive way to ask questions and get rid of the junk in, junk out—the problem that vexes health care economics.

And this is for the first pillar, which is focused on the curation and aggregation of real-world evidence, which enables practitioners look at ongoing treatment and outcomes data and get a well-rounded picture?

DH: It is, and that well-rounded picture is a broader view. So, understanding what is the cost of mitigation of side effects, for example. When a cancer drug is approved, there are generally two metrics: what percent of the population responded and what was the survival benefit.

And often it stops there. Physicians really don't understand much more. But if a drug actually causes infections or anemia that needs to be managed in-patient, the whole concept is, that is also the cost of the drug; that is also the cost of the intervention, and rarely are these things in oncology any way fully captured.

In many ways, I think this borrows from the progress of volume to value as it relates to bundles and things like that. It's really taking it quite seriously and understanding it and that learning, when, if these things are known, then a physician can balance the benefits and the risks across their choices of intervention.

But without this information, you're just guessing and it's anecdotal, and maybe publication-by-publication, but that's not an efficient way for information to transfer through the system.

Right, and that sounds like it would tie into the third product program, which focuses on patient-reported outcomes.

DH: Yes, exactly. In some ways, I would say the first one is the umbrella of two of the others, so maybe we can walk through and they'll piece together.

The "value-based era" is the economic impact that I was talking about, because we will be able to partner and put an overall cost of care beyond just the drug-gene-indication rubric of precision medicine.

So one of the things precision medicine really needs to do is stop being so exceptional and play by the same rules as any intervention in healthcare. Because of its novelty or its potential, it sort of has been given a bit of a pass for its early nascent years.

So this is, I think, a sign of the field maturing, where it's being beholden to any of the economic measures that any intervention would be held to. In some ways, its exceptionalism, I believe, has hindered its greater uptake and potential, because no one ever measured this in the way that other things would be traditionally measured.

Some of these economic measures that you say are a sign of the field maturing, do they apply to the provider end as well as on the patient end? For the provider, it's making sense of what to offer, and for the patient, it's figuring out what is cost effective?

DH: Right, the full purview of it. Unfortunately, cancer tends to be very episodic. And so I think this leads us also to the outcomes and patient reported outcomes piece.

Maybe we can transition into that side, which is, if you're looking for a greater picture with greater resolution, as well as a deeper understanding of the economics, you also need to understand as cancer patients live longer, we are seeing, I would say, a fortunate unintended consequence, which is what is the long term type of care and impact of quality of life of some of these very powerful interventions, many of which are brand new as it relates to mechanism of action.

I think you have to back up a moment and realize that immunotherapies, CAR-T, some of the viral vectors that are now being used there have not been long term studies in terms of any long term issues that may come from this, because no one's ever been long term, so I think this is also a very mature way of looking at it.

As someone who is interested in, what are the long-term immunologic or gastrointestinal issues that can follow a successful treatment within immunotherapy, you need a patient to tell you how they're doing, because we simply don't know outside of the clinical trial realm, which is very episodic.

So I would say what we're trying to do is extend the view of the impact of these medicines far outside of the acute care setting or the clinical trial setting in order to have a more full understanding of the risks and benefits.

If you take the first concept, which is we're measuring all along the way in a common system, we can then do comparisons to understand how these things occur. Some of the benefits tend to be the amount or depth of information, the genetic markers, be it economic, and then the other dimension of it is looking at the total lifecycle or extending the episode of care so that we more fully understand the impact of the medicines or risks.

And we're not just talking about effectiveness, right—because that's simply how it translates beyond the trial setting—but also quality of life and long-term adverse outcomes?

DH: That's right. And again, I think an important part for us is to back up and realize that these are drugs with new mechanisms of action. It really is an incredible time of innovation and pharmaceutical development, and this is all on the shoulders of understanding the biology as elucidated by the genome and all of the research that's gone on in the 17 years since the genome was published.

We understand the biology relatively well. What we don't understand is the full medical picture of the intervention and this gets us to that.

The final product program is, obviously, taking patients beyond just matching to clinical trials by improving the enrollment process.

DH: Right. You know, there is a point where waste in health care benefits nobody. There is no entity in this ecosystem that benefits from the waste.

So if we are able to speed drug development with greater precision on which patient goes on which trial, there are operational benefits on the site side, meaning our coordinators simply do less work in order to accomplish their goals, which is access to experimental medicine in the community setting. That's very important to see at CHI and Dignity.

These sorts of information systems, we use every day in our lives, but very few times have we harnessed that together with the goal that really is aimed towards oncology clinical trial development. Everyone benefits when the right patient is put on the right trial. It decreases the cost of drug development; it decreases the cost of running a site-side research program.

Again, when you eliminate waste from the system, the benefit is primarily to the patients and there are peripheral economic benefits later. Hopefully this could impact the overall cost of drugs, although I will put an asterisk and say that's speculative.

But theoretically, everyone can agree that information can drive better decisions that make the overall system more streamlined, and we are certainly in need of those things. So when you look at all the dimensions that can help the efficiency and impact of medicine, understanding biology of the patients is a very large piece of this.

So, what is that contribution to it and how do we unpack that so as to make our clinical decisions policy decisions? I would say the first wave in precision medicine was, every drug was unique, meaning each mechanism of action in the drug-gene-indication matrix, each one was a new entity that could solve a problem.

Now we're comparing across and within drug classes, there are drugs competing against each other, and to understand who goes on what, when is it worthwhile to run a trial, and if we truly believe that we're moving into an era in which molecular mechanism of tumor is as important as what tissue it came from, then you really need to be able to prove that and you can't do it with thousands of randomized studies asking one question each. You really have to be able to use it to weave clinical research into the fabric of community cancer care so that you're asking the questions as you're looking for the solutions. These platforms allow that.

There is such a strain on resources to stay current, and it is not possible for someone to be able to effectively perform at the quality levels they want with the RVU-like systems and the physician-scientists keeping up with every primary publication. It is it is not possible. The complexity is way too far in this field.

With this new suite of tools slated for development and subsequent integration into Syapse, how robust will the platform be compared to other clinical decision support programs in oncology?

DH: As important as the core technology is, it's about bringing the ecosystem together. And Syapse has been effective in doing this on a common platform. For example, they support the TAPUR trial and so they're starting to connect the dots from industry, drug developers, obviously molecular diagnostics, groups like mine that bring to bear a cohesive strategy to hundreds of cancer care providers. And then you're able to leverage that with payers and other groups in order to give that broader picture and deeper understanding.

I would say there's a lot of noise going on as this industry matures and to really bring together the right constituents in the ecosystem and have them communicate in an honest way is reflective back to some of the things that [former Vice President] Joe Biden said, and these things happening in a very real way.

You could give all the power points in the world until you bring these people together and we're able to look at a cohesive single source of truth. Without the data, you're never going to get anywhere.

How does Syapse help facilitate interactions with payers and bring them to the table? How does it make your work as a provider easier?

DH: That's a great question. Payers want to know, "Will this intervention be worth it?" And what is the total picture as it relates to the benefit of any given pharmaceutical. I would envision that as it relates to Roche and their portfolio, the uninformed payer is a barrier to patient access.

The agreement to come together to get a better measurement of impact in value will eventually lead towards giving the necessary information that allows for coverage determinations and patient access.

That is, with the host of payers that any major health system would be negotiating with?

DH: That's right. I mean, these tend to be often first announced by the CMS, and you see patient access basically coming off of analyzed data that can help with coverage determinations. But without the information to guide that, you can't even approach the process.

So, one of the keys here is, the resolution of healthcare is often proximal to the quality of the EMR systems and clinical informatics. This is in a way improving that resolution so that you can ask better questions and have more sure answers.

Did I miss anything?

DH: No, I really do think that the concept of eliminating waste from the health care ecosystem benefits everybody. And so that's why this sort of hackneyed concept of bringing everyone to the table—that all sounds great. This is actually doing it.

When we last spoke a-year-and-a-half ago, the Moonshot was at a high point, and everyone was laying out blueprints for how things should be done. The field seems to be in implementation mode now.

DH: I'm actually the keynote speaker at the Precision Medicine track for HIMSS [Healthcare Information and Management Systems Society Annual Conference and Exhibition]. I'm going to be sharing my experience about, a year-and-a-half ago, some people get in a room and I say let's work on this, right? What happens next?

And I think, when we last spoke, it was all very conceptual. I'll tell you very little strategically has changed. When I pull up the strategic documents from a year-and-a-half ago, I think we had a pretty good understanding of where this was going to go. The progress with providers is what we are most proud of in a short amount of time.

I would say developments like what happens with Roche and Syapse—that helps. It's almost as if the thing, the concept that we're trying to bring forward actually has more meat on it and it's much more mature, and all the more reason to have an active management strategy on this facet of medicine. Really, really exciting.

And this is moving rapidly in the community setting, no longer just within academic oncology.

DH: That's right. Some of the Precision Medicine Alliance's concepts is to be a fast follower and postmodern in a way that I don't actually need to build or own everything. It's about access. And if you look at it from an industrial level at the scale that we're trying to launch, I would rather bring 95 percent of our patients an 80 percent solution than a 100 percent solution to 2 percent of our patients.

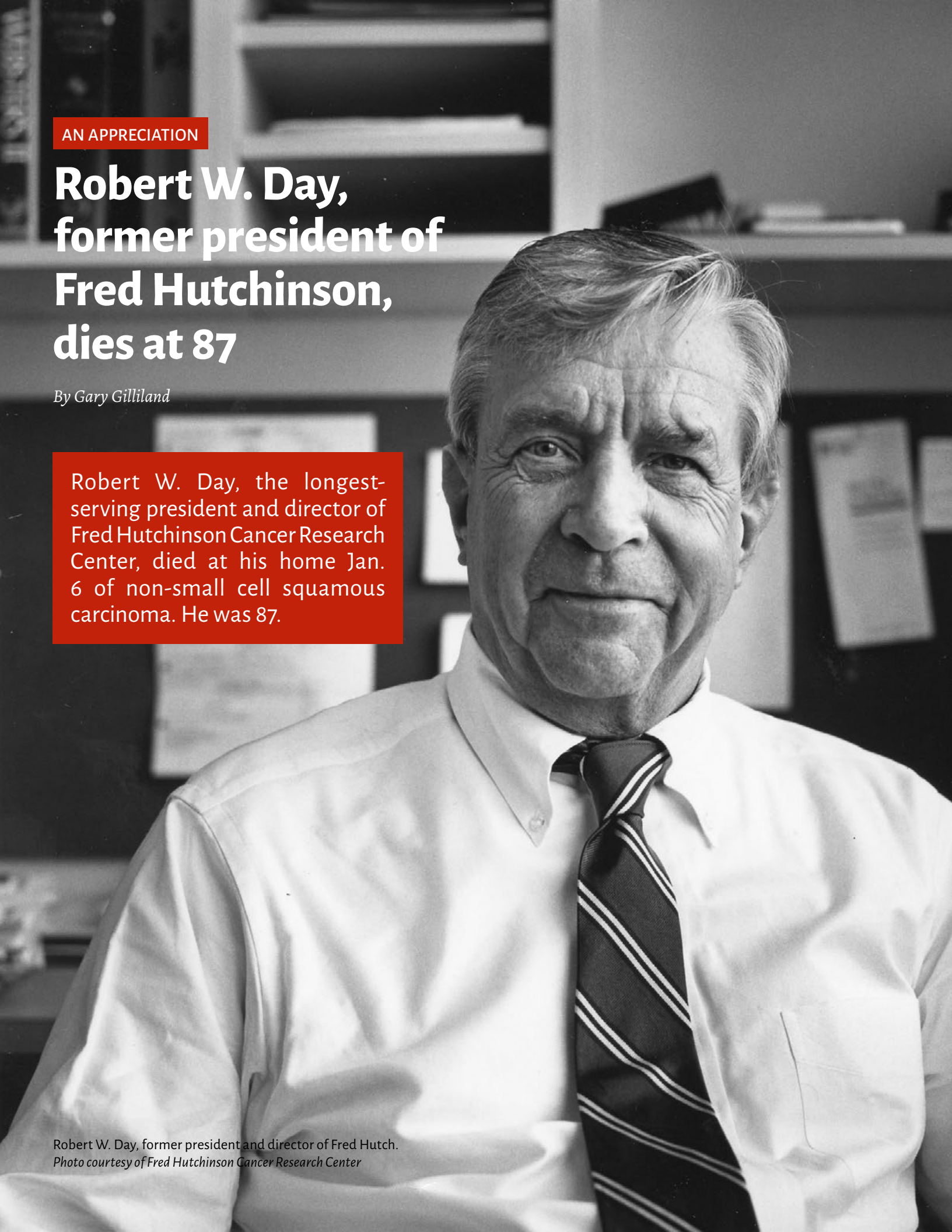
This really has to do withs access and these things just to make the overall field more impactful and equitable, because we know what we're doing better and there's better reason to strategically invest in it.

AN APPRECIATION

Robert W. Day, former president of Fred Hutchinson, dies at 87

By Gary Gilliland

Robert W. Day, the longest-serving president and director of Fred Hutchinson Cancer Research Center, died at his home Jan. 6 of non-small cell squamous carcinoma. He was 87.



Robert W. Day, former president and director of Fred Hutch.
Photo courtesy of Fred Hutchinson Cancer Research Center

As the current president and director of Fred Hutch, I personally will be forever grateful to Bob for taking me under his wing when I started here three years ago. He was a wonderful friend and mentor to so many of us, and his passing is mourned by all.

He struggled with cancer for many years, but one would never have known it to see him in action. He was such an inspiration in this, as in all things, showing extraordinary strength and courage that matched his wisdom.

Among his many accomplishments as a public health researcher and cancer center leader, one in particular stands out for all of us at the Hutch. Our center's campus was brought into being under his leadership. Moving Fred Hutch from its original location in Seattle's First Hill neighborhood to our current home at the south end of Lake Union was one of the most important and momentous decisions in the history of the Hutch.

A bronze bust of Bob now sits at the center of the campus that he made possible. Soon after I shared the news of his death with my colleagues, flowers began collecting at the statue's base.

Bob's influence extended far beyond the Hutch, but he always found time, long after stepping down as president, to devote to this organization and, especially, the people here. What follows are excerpts of our tribute to Bob, written by our staff and published shortly after his death.

Day presided over the Hutch from 1981 until 1997, a period when E. Donnall Thomas' pioneering bone marrow transplant research drew increasing international attention and earned Thomas the 1990 Nobel Prize in Physiology or Medicine.

A well-read man gifted with charm and wit, Day was also a competitive and uncompromising advocate, determined to fulfill his vision of the Hutch—that of a growing, thriving center of excellence for basic science, clinical trials, public health and prevention research. Under his leadership, Fred Hutch established its long-standing position as the top recipient of research grant dollars from the National Cancer Institute.

But Day's signature achievement was acquisition of land in Seattle's South Lake Union in a series of transactions from 1988 through 1991 and the subsequent move from the Hutch's original headquarters on Seattle's First Hill to a 15-acre complex now known as the Robert W. Day Campus.

“A bronze bust of Bob now sits at the center of the campus that he made possible. Soon after I shared the news of his death with my colleagues, flowers began collecting at the statue's base.”

– Gary Gilliland

Research on the campus continues to thrive, room for growth remains, and the Hutch campus today anchors a once run-down South Lake Union district that has become a global center for the convergence of bioscience and information technologies.

Day was an enthusiastic tennis player, skier and angler, but his real passion was for books. Growing up outside Boston in Framingham, Mass., he was drawn to the local library, inspired by an older sister who became a scholar and librarian. He later found a refuge as a Harvard student in the undergraduate library there. “It was just wonderful, and I spent hours at the place,” he told a friend. “It was my education, really.”

Day left Harvard early, transferring to the University of Chicago Medical School, attracted in part to the educational philosophy of the university's president, Robert Maynard Hutchins, a proponent of teaching the Great Books of the Western World. As a student, Day attended small, informal dinners at the university with the likes of physicist Enrico Fermi and economist Milton Friedman. He graduated in 1956 with an M.D. and an intense interest in public health.

His academic training and early career in public health forged a commitment that would later shape the Hutch as a leader in the field. Before coming to Seattle in 1969, he was already a rising young star, serving as chief deputy director of the California Department of Public Health under the administration of then-Gov. Ronald Reagan.

Day spent nearly a decade as dean and professor at the University of Washington School of Public Health. He was a UW representative on the Fred Hutch board when founder Dr. William Hutchinson reached out in 1981 and asked him to run the center.

Day was the first to succeed the iconic Hutchinson as president and director, and as such he had enormous shoes to fill. A Seattle celebrity himself, “Dr. Bill” had shepherded the growth of

his cancer center from the start and named it in memory of his younger brother, the legendary Major League Baseball pitcher and manager Fred Hutchinson, who died in 1964 of cancer at the age of 45.

As Fred Hutch's president, Day quickly set about creating his own administrative infrastructure, making his mark with a disciplined hand and a strategic outlook. Facing competition for that talent from new biotechnology companies, and convinced that the Hutch needed room to grow, Day soon began looking to consolidate all Hutch operations, which were spreading to downtown Seattle.

That search led him and his team to a neglected neighborhood of warehouses, apartments and light industry at the south end of Lake Union. After acquiring the land from 37 different interests—the largest assemblage of property in the city of Seattle since the World's Fair of 1962—Day launched what became a 10-year process of moving to new quarters.

"The thing that sticks in my mind about Bob Day was that, if he had trust and confidence that you could do your job, he would allow you to do it, no strings attached," said Guy Ott, a retired Hutch vice president who was responsible for executing the difficult transition to the new campus. "He told you what needed to be done, gave you the resources to do it, and then got out of the way."

"The thing that sticks in my mind about Bob Day was that, if he had trust and confidence that you could do your job, he would allow you to do it, no strings attached, He told you what needed to be done, gave you the resources to do it, and then got out of the way."

– Guy Ott

In the final years of his presidency, as the phased construction of the new campus was under way, Day oversaw the complex negotiations with the University of Washington and Seattle Children's Hospital that led to the creation of Seattle Cancer Care Alliance, the clinical care partner of Fred Hutch.

After passing the reins in 1997 to Fred Hutch geneticist—and future Nobel laureate—Dr. Lee Hartwell, Day remained on the faculty, continuing to conduct his own research. Notably, he led ongoing studies of the impact of the Chernobyl nuclear power plant disaster on childhood leukemia. He also became involved in business, co-founding Orca Biosciences, a developer of diagnostic blood tests for early detection of cancer, which in 1999 merged with the German firm Epigenetics AG.

In 2005, Day and his wife, C.J. Taylor-Day, founded the Science and Management of Addictions Foundation, with a mission to eliminate the disease of substance addiction in youth by advancing research education and treatment. C.J. died in 2011 after an eight-year battle with ovarian cancer.

He is survived by the couple's two daughters, Natalya Bennett, of Riverview, Florida, and Julia Webb, of Mountlake Terrace, Washington; and by his first wife, Jane Day, and their daughter, Nate Tatum, of Quilcene, Washington, and their son, Christopher, of Seattle; and two grandchildren.

The author is the president and director of Fred Hutchinson Cancer Research Center.

AN APPRECIATION

Marsha Fountain Woznuck, nurse and pioneering cancer center administrator, dies at 65

By Catherine Harvey Sevier

Marsha Fountain, retired president of The Oncology Group, died Jan. 7 after a long struggle with metastatic breast cancer. She was 65.

Marsha's career began in the early 70s as a pediatric oncology nurse at MD Anderson Cancer Center. She quickly moved into the then "new" field of cancer program administration at a time when the field was learning how to consolidate cancer services across the continuum. Working in health systems in three states, and with colleagues including Gayle Katterhagen, Marsha became a "go to" person for new administrators learning the ropes.

In the late 1990s, after nearly two decades in the trenches, she became vice president of the Stichler Group, an architecture and design firm with expertise in hospital design. While there, she focused clients and planners on the importance of patient-centered space that provided for a comfortable and therapeutic experience.

From the 2000s until her retirement in 2015, she served as a cancer consultant working with cancer centers, networks, and hospitals to develop, evaluate, and operationalize their programs and services. She was a founding partner and later president of The Oncology Group.

Marsha was very generous and committed to sharing her knowledge with others. She was a nationally recognized breast centers expert and served on numerous boards and as a resource to many organizations. She was a founder of the American College of Oncology Administrators and was the first president of Association of Cancer Executives.

As Marsha's former business partner and friend, I cannot overstate the contributions she made to the field. She was committed to the care and well-being of all those living with cancer and was a true advocate for them. For those of us who had the privilege of working with her, we knew her heart for others, her willingness to go the extra mile, and her loyalty as a friend. She will be sorely missed.

She is survived by her husband, Steve; stepson, Jason; sister, Sandra (Al); brothers-in-law, Larry, Paul (Nancy); nephews, Greg (Nickie), Brad (Jim), Robert, Jacob (Alex) and niece, Hannah; great-nieces and nephews; Aunt Sherry Smith; and numerous beloved cousins and lifelong friends.

Memorial service: 10:00 A.M. Feb. 17, at Marty Leonard Community Chapel, 3131 Sanguinet Street, Fort Worth.

In lieu of flowers, the family asks for donations to:

Azle Senior Center
601 Southeast Parkway,
Azle, TX 76020

or

Simmons Cancer Center
at UT Southwestern
PO Box 910888
Dallas TX 75391-0888.

The author is the managing director of The Generations Study Group, a consulting group

IN BRIEF

Emory receives $400 million pledge from Woodruff Foundation

A $400 million pledge to Emory University from the Robert W. Woodruff Foundation will be used to construct a Winship Cancer Institute Tower in Midtown Atlanta and a new Health Sciences Research Building on Emory's Druid Hills campus.

The Winship Cancer Institute Tower in Midtown will house a full range of outpatient cancer services.

The new Health Sciences Research Building on Emory's Druid Hills campus, a laboratory-focused facility, will house faculty and staff who are charged with developing a pipeline of cures, interventions, and prevention methods, all aimed at improving the health of patients.

Research teams will partner with Emory colleagues to target five emerging priorities in 21st century medicine: cancer; brain health; heart and vascular health; immunology and infectious diseases; and radiology, biomedical engineering, and imaging sciences. Emory's partnerships also include Children's Healthcare of Atlanta.

Children's Mercy Kansas City receives gifts—totaling $150 million

Two of Kansas City's families joined together to donate $150 million to Children's Mercy Kansas City.

Their gift constitutes the largest one-time gift ever made to a children's hospital for pediatric research, the Hall Family Foundation and the Sunderland Foundation each donated $75 million to kickstart the construction of the future home of the Children's Research Institute and accelerate the recruitment of top researchers from around the globe.

Located on the hospital's Adele Hall Campus in downtown Kansas City, the new research building consists of a nine-story structure making up approximately 375,000 square feet. As a result, the Children's Research Institute will house nearly six times more space for pediatric research than currently exists at Children's Mercy. When fully staffed, Children's Mercy will grow its research enterprise tenfold as a result of this donation—with everyone striving to find much-needed answers for kids and their families.

"We have an opportunity to change the lives of children by conducting research that will create more understanding and deliver cures or diagnostics that go beyond the individual patient," said Tom Curran, chief scientific officer at Children's Mercy Kansas City, executive director of the Children's Research Institute and the Donald J. Hall Eminent Scholar in Pediatric Research. "So, in a sense, by treating one child here at Children's Mercy, we may impact thousands elsewhere."

Several of the windows are a different color from the rest. Those windows represent the genetic anomalies found in the DNA of children with specific rare diseases – just some of the difficult cases and questions the researchers inside the building are trying to solve.

The Hall Family Foundation was founded in 1943 by Joyce and Elizabeth Hall, along with Joyce's brother Rollie B. Hall, to promote the health, welfare and happiness of school-age children; the advancement and diffusion of knowledge; activities for the improvement of public health; and advancement of social welfare.

The Sunderland Foundation (formerly the Lester T. Sunderland Foundation) was established in 1945 by Lester T.

Sunderland, who served as president of Ash Grove Cement Company for 33 years. Ash Grove Cement, which the Sunderland Family recently sold to CRH plc in Dublin, Ireland, is considered the largest cement company in the U.S.

Mary Beckerle receives NCI Knudson Award

Mary Beckerle, CEO and director of Huntsman Cancer Institute at the University of Utah, is this year's recipient of the Alfred G. Knudson Award in Cancer Genetics from the NCI.

The award is named after Alfred G. Knudson, a physician and researcher whose work added major insights to the understanding of the genetic basis of cancer. The award is presented by the NCI each year to a scientist who has made significant research contributions to the field of cancer genetics.

Beckerle will receive the award and present the award lecture, "Interface Between Cytoskeletal Dynamics and Tumor Biology" at NCI.

Beckerle's research has discovered a new pathway that is critical for the ability of cells to respond to mechanical signals in their environment. Such signals are now known to regulate cell growth and movement, two behaviors that are critically important in tumor biology.

Her lab is currently focused on understanding the impact of this pathway on tumor progression, particularly in Ewing sarcoma, a rare but deadly bone cancer that typically affects children and young adults.

In addition to leading HCI, Beckerle is a distinguished professor of biology and oncological sciences and holds the Jon M. Huntsman Presidential Endowed Chair at the University of Utah.

Beckerle was appointed as a member of Vice President Biden's Cancer Moonshot Blue Ribbon Panel where she co-chaired the working group on Precision Prevention and Early Detection. Beckerle is an elected Fellow of the American Academy of Arts and Sciences and the American Philosophical Society.

Beckerle is the 22nd Knudson award winner. Past recipients of the award include Nobel laureates J. Michael Bishop, Robert Horvitz, Harold Varmus, Leland Hartwell, and Elizabeth H. Blackburn.

Chi Van Dang as editor-in-chief of AACR journal Cancer Research

Chi Van Dang was named editor-in-chief of Cancer Research, a journal published by the American Association for Cancer Research.

Dang is the scientific director of the Ludwig Institute for Cancer Research, an international, not-for-profit organization of distinguished scientists dedicated to preventing and controlling cancer. He is also a professor in the molecular and cellular oncogenesis program at the Wistar Institute.

Dang's lab was the first to report a link between an oncogene and altered cancer cell metabolism through the discovery that the oncogenic transcription factor MYC plays a pivotal role in the re-programming of fuel utilization in cancer cells, making cancers addicted to certain fuel sources. Research in the Dang laboratory currently focuses on exploiting metabolic vulnerabilities of cancer cells for therapeutic benefit.

Dang is the chair of the National Cancer Institute's Board of Scientific Advisors, a member of the Blue-Ribbon Panel of former Vice President Joe Biden's National Cancer Moonshot Initiative, a fellow of the American Academy of Arts and Sciences, and a member of the National Academy of Medicine.

Mark Israel named executive director of Israel Cancer Research Fund

Mark Israel, a pediatric oncologist and translational scientist, was appointed national executive director of the Israel Cancer Research Fund, a nonprofit organization dedicated solely to funding cancer research in Israel.

Israel joins ICRF from the Geisel School of Medicine at Dartmouth College, where he is a professor in the Department of Pediatrics, Medicine, and Molecular and

Systems Biology. From 2001 to 2016, Israel served as the director of Dartmouth's Norris Cotton Cancer Center.

For the last 12 years, Israel has been a volunteer member of the ICRF's scientific review panel and the chair of the panel that evaluates translational cancer research proposals.

"Cancer research has never been more exciting or promising—and that is particularly true in Israel," Israel said in a statement. "Israeli science knows no bounds. ICRF provides a singular opportunity to help build more recognition and support for the world-class cancer research of Israeli scientists, and to arm and empower its finest practitioners with the resources necessary to change the world."

International Association for the Study of Lung Cancer becomes member of registry of real-world data

The International Association for the Study of Lung Cancer has become a member of the Lung Cancer Patient Registry.

IASLC joins the Bonnie J. Addario Lung Cancer Foundation and the American Lung Association's LUNG FORCE, the registry's current member organizations.

The registry's objective is to provide a real-world view of patient outcomes and treatment effectiveness. Lung cancer patients enter information anonymously into the Registry. Registered patients, their families, health care providers, and researchers can access that information.

The registry enables registered researchers to query de-identified data in any combination of data elements using the research portal online search tool. Researchers interested in submitting proposals for placing clinical trials within the Registry may now submit a proposal.

"Anytime patients and doctors can collaborate more effectively, we improve the experience for both," said Fred R. Hirsch, CEO of the IASLC. "As a global, multidisciplinary organization with a mission to conquer lung cancer, we look forward to the collaboration and the impact of the Lung Cancer Registry and are thrilled to join the partnership."

This month, the Lung Cancer Registry will launch a study on the side effects of immunotherapy on non-small cell lung cancer patients using data provided by patient participants.

Patients with any form or stage of lung cancer can join the Registry at www.lungcancerregistry.org. Patients can opt-in to contribute their information, set their contact preferences and compare their lung cancer experience with others in The Registry. Patients can choose to receive information about research opportunities or other relevant news as part of their participation.

Elizabeth Barrett named CEO of Novartis Oncology

Elizabeth Barrett was appointed CEO Novartis Oncology and a member of the executive committee of Novartis.

Barrett is currently Global President Oncology at Pfizer Inc.

Barrett succeeds Bruno Strigini who is retiring from Novartis for personal reasons, the company said.

Barrett's appointment is effective Feb. 1, and she will be based in Basel.

In her most recent role at Pfizer, Barrett led the oncology business through a significant period of growth achieved in less than three years. Before joining Pfizer in 2009, she worked at Cephalon Inc. and Johnson & Johnson. She started her career at Kraft Foods Group Inc. in 1984.

Novartis also announced today that Robert Kowalski, head of global regulatory affairs, will assume ad interim leadership of the drug development organization effective Feb. 1. Kowalski has been head of global regulatory affairs for Novartis since February 2016 and has played an important leadership role in securing approvals for several breakthrough medicines including our revolutionary CAR-T therapy Kymriah, the company said.

FUNDING OPPORTUNITIES

LUNGevity issues RFA for 2018 Career Development Award in translational research in lung cancer

LUNGevity Foundation has issued a Request for Application for translational research in lung cancer for the 2018 Career Development Award.

LUNGevity Career Development Awards support future research leaders who will keep the field of lung cancer research vibrant with new ideas.

The award, for translational early detection or therapeutics projects, including immuno-oncology projects, is open to junior faculty members who are within the first five years of their first faculty appointment.

Successful applicants may receive up to $100,000 per year for a possible period of three years and will participate as ex officio members of LUNGevity's Scientific Advisory Board for the duration of the award. LUNGevity will grant only one Career Development Award per institution.

The Requests for Applications will be posted as of Jan. 16, 2018, on the LUNGevity website and on the proposalCENTRAL website.

For more information, contact Margery Jacobson at mjacobson@LUNGevity.org or 312-407-6109.

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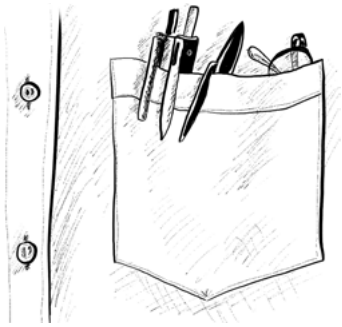

TRIALS & TRIBULATIONS

How disease-specific clinical trial finders can address gaps in study participation

By David F. Arons
Chief Executive Officer of the National Brain Tumor Society

As a cancer patient advocacy organization—especially one dedicated to a category of malignancies that have seen frustratingly slow progress and only negligible improvements in survival rates over the past four-plus decades—we've come to view our role and responsibility to the brain tumor community as something like that of a plumber.

That is, we look across the neuro-oncology drug discovery and development "pipeline" and search for bottlenecks, blockages, and obstacles impeding the path to accelerated progress. We then design programs aimed at plunging away those jams and allowing the entire neuro-oncology R&D system to function more effectively.

Unfortunately for us, the queue in this regard is quite lengthy and spans the entirety of the pipeline, from knowledge gaps in basic science, to model gaps in preclinical research and measurement gaps in response assessments during clinical research. Most will require major commitments of research-funding and projects that necessitate years of work; work that will remain ongoing. However, one easily identifiable area of need across all of oncology—but perhaps more pronounced in a rarer cancer like brain cancer—that also has, we believe, a relatively simple answer is the issue of clinical trial enrollment.

In a survey of more than 1,000 brain tumor patients, survivors, and primary caretakers (of which full results were presented at the 2017 Annual Meeting of the Society for Neuro-Oncology last November), the National Brain Tumor Society (NBTS) found that only 42% of respondents indicated their medical team talked to them about clinical trial enrollment. In other words, far too

many brain tumor patients are never informed of their clinical trial options.

These results fueled our interest in creating a better, simpler, and more user-friendly trial finder tailored specifically for brain tumor patients. Fortuitously—or rather, serendipitously—for us, a brain tumor survivor who happened to have experience and expertise in creating custom trial finders was getting the same itch. Michael Wenger, a brain tumor survivor and web development expert, offered to work with our research staff and volunteer his time to build NBTS a custom, brain tumor-specific clinical trial finder.

Like all cancers, malignant brain tumors—or "brain cancer"—are really a collection of a heterogeneous diseases that are each uniquely their own. And like many other cancers, the nomenclature for these individual entities can sound foreign to anyone unfamiliar with the disease or without a medical degree. Glioblastoma, diffuse intrinsic pontine glioma, acoustic neuroma, craniopharyngioma, schwannoma, oligodendroglioma, subependymal giant cell astrocytoma—these are some of the approximately 140 distinct types of brain tumors.

Now, imagine the emotion, confusion, and shock that overwhelms them and their loved ones. They've just been diagnosed with a potentially life-threatening disease for which they can't even pronounce or spell the name of, the doctor is recommending invasive and risky brain surgery within 48 hours, and their life is turned frantic. And we expect them to have the wherewithal to stumble upon ClinicalTrials.gov? And then know how to fill in the appropriate information and review the results accordingly? Not likely.

Yet, this is a critical juncture for a patient's treatment decision-making. Begin treatment and you could automatically exclude yourself from a number of trials that require no prior treatment to enroll, including many "newly diagnosed" trials. However, these trials testing the latest, most-informed potential new treatments and emerging medicines may be that patient's best chance at survival.

While the National Library of Medicine, which administers ClinicalTrials.gov, can never be expected to do the level of promotion required to break through the chaos of a new diagnosis in individual patient populations, patient advocacy groups are uniquely positioned, and have the culture, understanding, and familiarity with their community to get in front of patients and caregivers earlier on in the disease experience. In this context, the resources—on-line and off-line—provided by patient advocacy groups can be "one-stop-shops" for information for newly diagnosed patients and their caregivers to get a holistic view of all their treatment options, including clinical trials.

Functionality for any trial finder does matter, too. Which brings us to the NBTS Clinical Trial Finder, and why we believe it is not only more likely to get in front of patients and caregivers, but, ultimately, easier for them to use, especially since it was developed by a patient himself. Patients are therefore quickly empowered to present their oncologist a list of viable trial options for their medical team to review.

To begin with the obvious, the NBTS Clinical Trial Finder—along with all other disease-specific trial finders—'shrinks the universe,' so to speak, for that patient population; searching and delivering a smaller pool of trials for patients to consider. In short, a disease-specific finder avoids boiling the ocean.

More important is the user interface, both in terms of getting started with the initial search screen and then with how results and individual entries are returned to patients or caregivers.

The NBTS Clinical Trial Finder presents potential trial volunteers with several key fields: zip code; distance willing to travel; age; sex; type of trial the user is looking for (healthy volunteer vs. patient & observational vs. interventional); and, of course, a keyword/tumor type. These fields are designed to return only trials within the geographic-range and specifications a patient is looking, and eligible, for.

On ClinicalTrials.gov, though the user interface is beginning to improve, the search fields first offered include: condition; other terms (with given examples being NCT number, drug name, investigator name); and country. There is an "Advanced Search" option, but with dozens of unintuitive fields, it hardly improves prospects for most newly diagnosed patients. Using the site's standard search feature, unlike the NBTS Trial Finder, patients would get back every trial for their tumor type in the United States, regardless of whether it was observational and they are looking for interventional; or if it's only open to healthy volunteers; or if it doesn't have any participating centers inside the range they'd be willing or able to travel; or if it excludes their age group. The practical implication of this for a newly diagnosed patient under great stress is that they are left with trial after trial to wade through, just to find the few that are actually feasible for them. The NBTS Clinical Trial Finder helps make this process more manageable.

Further, when search results are returned our finder first presents a simple summary of trials to scroll through (fig. 1). ClinicalTrials.gov returns a list with little key information readily identifiable for a patient or caregiver (fig 2). And when you click to view an individual entry, in our finder you are shown a clean, easy to view page featuring information on (top-to-bottom): Trial Purpose, Recruitment Criteria, Trial Details, and Contact info (with a sidebar running on the right side of the page containing info on the nearest location and site contact phone number).

HIF-2 Alpha Inhibitor PT2385 in Treating Patients With Recurrent Glioblastoma

This phase II trial studies how well HIF-2 alpha inhibitor PT2385 works in treating patients with recurrent glioblastoma. HIF-2 alpha inhibitor PT2385 may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth.

18 Years and Over

Dana-Farber/Harvard Cancer Center at Dana Farber Cancer Institute (36 mi away)

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INdividualized Screening Trial of Innovative Glioblastoma Therapy (INSIGhT)

This research study is studying several investigational drugs as a possible treatment for Glioblastoma (GBM). The drugs involved in this study are : - Abemaciclib - Temozolomide (temodar) - Neratinib - CC115

18 Years and Over

Massachusetts General Hospital (34 mi away)

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FMISO PET Study of Glioblastoma

In this research study, the investigators are using FMISO-PET and MRI scans to explore the delivery of bevacizumab to the blood vessels in patient's with recurrent glioblastoma before and after treatment. Bevacizumab is approved by the U.S. Food and Drug Administration for use in patients with recurrent glioblastoma . It works by targeting a specific protein called VEGF, which plays a role in promoting the growth or spreading of tumor blood vessels. Since anti-VEGF agents also affect normal blood vessels in the brain, they can inhibit the way other drugs used in combination with bevacizumab are delivered to the tumor. In PET scans,...

18 Years and Over

Massachusetts General Hospital (25 mi away)

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FIGURE 1

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	INtraoperative photoDYnamic Therapy of **Glioblastoma**	**Glioblastoma**	• Device: "perPDT" • Drug: GLIOLAN	• Hôpital Roger Salengro, CHRU, Lille, France
2	☐	Recruiting	INdividualized Screening Trial of Innovative **Glioblastoma** Therapy (INSIGhT)	**Glioblastoma**	• Drug: Temozolomide • Drug: Neratinib • Drug: CC-115 • Drug: Abemaciclib	• University of Alabama at Birmingham, Birmingham, Alabama, United States • Massachusetts General Hospital Boston, Massachusetts, United States • Dana Farber Cancer Institute Boston, Massachusetts, United States • (and 7 more...)

FIGURE 2

For ClinicalTrials.gov entries, entries are a significant degree more convoluted, busy, and harder to parse through for prospective volunteers. Here is an example.

And these improvements only begin to scratch the surface of what can be done to make the clinical trial education and search process more optimal for patients. Moving forward, it's critical that we continue to tackle 'blindspots' that exist in current, general clinical trial finders like ClinicalTrials.gov. For example, our next upgrade to the NBTS Trial Finder that is under development will be the functionality for potential volunteers to save their searches/search criteria and be notified when new trials are posted that match their criteria, so that the onus isn't on patients and caregivers to continually check back and re-run their search.

Ultimately, disease-specific clinical trial finders—combined with other resources and information that aide treatment navigation—could do more than simply help empower patients to take greater control over their treatment decision. We envision a future where patient advocacy organizations—who are increasingly experimenting with creating their own patient registries—could couple a trial finder with a patient registry to pre-qualify patients for trial enrollment, creating a paradigm that stands to vastly increase the amount and speed of trial participation and enrollment, respectively.

In the interim, patient advocacy-run trial finders can begin to patch a leak in the cancer R&D pipeline by identifying and addressing blind spots in current options like ClinicalTrials.gov. The strides the NLM and NIH are making with that finder are commendable, but, in general, ClinicalTrials.gov will continue to best cater toward more of a research or professional audience. Disease-specific finders better meet the specific and unique needs of individuals who are new to the harrowing experience as a cancer patient and are likely on the fence about their treatment options, and particularly whether or not to volunteer for a clinical trial of an unproven therapy.

In just eight months since the launch of NBTS Clinical Trial finder more than 31,000 searches have been conducted by 640 unique visitors from 96 countries. The demand is clear. As we continue to refine and promote the trial finder, we're confident that the number of patients and their caregivers utilizing this resource will allow more patients to access cutting-edge, potentially life-saving treatments, while allowing trials to move forward quicker through increased and more rapid enrollment of patients from this community.

The author is the chief executive officer of the National Brain Tumor Society. In 2016, Arons served on the Blue Ribbon Panel of experts selected to advise Vice President Joe Biden's Cancer Moonshot initiative. National Brain Tumor Society is the largest nonprofit organization dedicated to the brain tumor and brain cancer community and cause in the United States.

CLINICAL ROUNDUP

Yale study demonstrates four-fold superiority of academic level diagnostic accuracy

Specialty diagnostics company Precipio Inc. announced preliminary data from an ongoing study on the impact of academic pathology expertise on diagnostic accuracy.

The purpose of the study was to independently evaluate the effect of academic pathology on the massive problem of misdiagnosis, and determine the impact of Precipio's business model as a solution to this problem.

Initial data shows that of the biopsy samples that Yale specialist pathologists provided a second opinion on and arrived at different diagnoses, ~73% arrived at a diagnosis that either definitely or possibly changed the patient treatment plans.

This is strengthening industry data on the problem of misdiagnosis, providing powerful evidence to the consequences to patient care, and validating Precipio's business model as the only innovative solution of its kind to combat the problem of misdiagnosis.

This data is further strengthened by the comparative data generated internally by Precipio, demonstrating that in the first 100 cases initially diagnosed by academic expert pathologists at Yale and then sent to an outside pathologist for a second opinion, in 99% of those cases, the second opinion confirmed the primary diagnosis arrived at by Yale.

The study's purpose, launched July 2017, is to evaluate the hypothesis that academic pathologists' expertise result in a higher rate of diagnostic accuracy than the current industry is providing. The study was designed to retrospectively evaluate the concordance in two sets of data in order to demonstrate this hypothesis.

The first cohort consists of patients who received their primary diagnoses non-academic community hospitals or national reference labs (representative of the industry), and were then referred to an academic pathology institution (Yale University) for a second opinion consultation. The purpose of evaluating this cohort was to re-assess the diagnosis received outside of an academic institution, and then have an academic expert specialist evaluate its accuracy.

The second cohort consists of patients initially diagnosed at Yale University, and then referred to another academic institution for a second opinion consultation, (for example at the Brigham & Women's Hospital in Boston, or at Memorial Sloan Kettering Cancer Center in New York).

The purpose of evaluating this cohort was to review the diagnosis rendered by an academic expert, and assess its accuracy by having it reviewed by a peer academic expert – thus, subject to the same scrutiny as the first cohort.

In the cases where there is a disagreement between primary diagnosis and the second opinion evaluation, the patient sample will be submitted to a third party academic institution to act as the arbiter (a process which currently does not exist in the industry).

For the purpose of this study, academic expert pathologists at University of Pennsylvania will review each of the discordant cases and determine the correct diagnosis.

Study investigators at Yale anticipated the first cohort would show a significant rate of misdiagnosis with meaningful consequences to the patient; while the second cohort would show minimal discordance, reflecting an overall substantially higher level of diagnostic accuracy rendered by academic pathologists.

To date, a total of 315 cases have been reviewed, 213 of which belong to the first cohort of the study, consisting of patients initially diagnosed at a non-academic facility, and then receiving a second opinion consult at Yale University.

The preliminary data reveals that, of the cohort of patients initially diagnosed at a non-academic institution, in 45 patients (21% of the cases) the academic pathologist arrived at a different conclusion during their second opinion assessment.

Furthermore, in 33 of those cases (>73%), the change in diagnosis had a potential substantial impact on patient treatment plan and is considered a material discordance.

In the remaining 102 cases reviewed that belong to the second cohort, in only 5% of the patients that were initially diagnosed by an academic expert, the second opinion diagnosis differed from the primary diagnosis. However, in 0% of those cases, did the change impact the patient treatment plan and is therefore not considered a material discordance.

The study will ultimately include at least 1,000 patients to further demonstrate the value of academic expertise in the diagnostic process. It is expected to be completed by the end of Q1-2018, after which the results will be compiled and published in a peer-reviewed industry journal.

Researchers demonstrate RAS dimers are essential for cancer

Researchers at UT Southwestern's Simmons Cancer Center have shown that RAS molecules act in pairs, known as dimers, to cause cancer, findings that could help guide them to a treatment.

The question of RAS dimerization has been debated, according to Kenneth Westover, assistant professor of radiation oncology and biochemistry with the Harold C. Simmons Comprehensive Cancer Center at UT Southwestern Medical Center.

The UT Southwestern team led by Westover used X-ray crystallography data to predict what a RAS dimer might look like, then tested the model in cells using a method called fluorescence resonance energy transfer to show when RAS forms dimers and when it does not.

The study, published in the journal Cell, provides a foundation for further studies that delve into RAS biology and could potentially pave the way to develop new cancer drugs that target RAS dimerization.

Members of the Westover research lab teamed up with researchers from the Dana Farber Cancer Institute to show that RAS dimers are essential in a number of cancer cell systems and animal models of cancer.

This work was supported by The US Department of Defense, V Foundation for Cancer Research, and the Cancer Prevention and Research Institute of Texas.

Xenoestrogens in foods may counteract breast cancer treatment

Scientists from The Scripps Research Institute discovered two estrogen-mimicking compounds found in many foods appear to potently reverse the effects of palbociclib/letrozole, a popular drug combination for treating breast cancer.

The study, published in the journal Cell Chemical Biology, suggests that exposure to xenoestrogens may significantly reduce the effectiveness of anti-estrogen treatments for cancer.

"Breast cancer patients taking palbociclib/letrozole should consider limiting their exposure to foods that contain xenoestrogens," says Gary Siuzdak, the study's senior author and senior director of TSRI's Scripps Center for Metabolomics.

The palbociclib/letrozole combination therapy was approved by FDA in 2015 after a clinical trial showed it doubled the progression-free survival time in postmenopausal women with estrogen receptor positive, metastatic breast cancer. The palbociclib/letrozole is one of the standard therapies for ER-positive breast cancers.

Siuzdak and colleagues, including first and lead author Benedikt Warth, then a visiting Erwin-Schrödinger Fellow in the Siuzdak Lab, used advanced metabolomics technology to analyze the effects of palbociclib/letrozole on breast cancer cells.

Their analysis revealed that neither palbociclib alone nor letrozole alone had a strong effect on metabolites in an ER-positive breast cancer cell line. However, the combination had a strikingly large impact.

Cancer researchers are increasingly concerned that xenoestrogens in food and water may enhance the growth of estrogen-fueled cancers, and may also hamper the effectiveness of anti-estrogen drugs such as letrozole. TSRI scientists therefore examined breast cancer cells treated with palbociclib/letrozole to see how their metabolite populations changed when they were also exposed to two common dietary xenoestrogens: zearalenone and genistein.

Zearalenone has been linked to birth defects and abnormal sexual development in pigs and other livestock, and is suspected of having caused an outbreak of early breast development among girls in Puerto Rico in the 1970s. Genistein is produced in certain plants including soybeans and is often highly concentrated in phytoestrogen-rich food supplements.

Even using very low doses, similar to typical dietary exposures, the researchers found that both model xenoestrogens largely reversed the metabolomic impact of the cancer drug combination.

Under the influence of either xenoestrogen, the breast cancer cells also resumed proliferating at a rate comparable to that seen in the absence of drug treatment. The results indicate that these dietary xenoestrogens do have the potential to affect cancer therapy outcomes—and genistein and zearalenone are just two of the many xenoestrogens commonly found in the human diet.

The impact of xenoestrogens on health and on hormonally-targeted therapies is nevertheless an understudied, underfunded area of research, the researchers emphasized.

Other co-authors of the study, "Metabolomics reveals that dietary xenoestrogens alter cellular metabolism induced by palbociclib/letrozole combination cancer therapy," were Philipp Raffeiner, Ana Granados, Tao Huan, Mingliang Fang, Erica Forsberg, and H. Paul Benton, all of The Scripps Research Institute at the time of the study; as well as Caroline H. Johnson at Yale University and Laura Goetz of the Scripps Clinic Medical Group.

Funding for the research came from the Austrian Science Fund (Erwin-Schrödinger fellowship awarded to Benedikt Warth), the George E. Hewitt Foundation for Medical Research and the National Institutes of Health (grants R01 GMH4368 and PO1 A1043376-02S1).

DRUGS & TARGETS

FDA expands indications for AZ's Lynparza, making it first treatment for breast cancer with BRCA mutation

FDA expanded the approved use of Lynparza (olaparib tablets) to include the treatment of patients with certain types of metastatic breast cancer whose tumors have a specific germline mutation.

Lynparza becomes the first PARP inhibitor approved to treat breast cancer. This is also the first time any drug has been approved to treat certain patients with metastatic breast cancer who have a BRCA gene mutation.

Patients are selected for treatment with Lynparza based on an FDA-approved genetic test, called the BRACAnalysis CDx.

Lynparza is sponsored by AstraZeneca Pharmaceuticals LP. BRACAnalysis CDx is sponsored by Myriad Genetic Laboratories Inc.

"This class of drugs has been used to treat advanced, BRCA-mutated ovarian cancer and has now shown efficacy in treating certain types of BRCA-mutated breast cancer," Richard Pazdur, director of the FDA's Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research, said in a statement. "This approval demonstrates the current paradigm of developing drugs that target the underlying genetic causes of a cancer, often across cancer types."

Lynparza was first approved by the FDA in 2014 to treat certain patients with ovarian cancer and is now indicated for the treatment of patients with BRCA-mutated, HER2-negative metastatic breast cancer, who have been previously treated with chemotherapy. Patients with HR-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine treatment.

In its most recent action, FDA also expanded the approval of the BRACAnalysis CDx, an approved companion diagnostic to Lynparza, to include the detection of BRCA mutations in blood samples from patients with breast cancer.

The safety and efficacy of Lynparza for the treatment of breast cancer was based on a randomized clinical trial of 302 patients with HER2-negative metastatic breast cancer with a germline BRCA mutation. The trial measured the length of time the tumors did not have significant growth after treatment (progression-free survival). The median progression-free survival for patients taking Lynparza was 7 months compared to 4.2 months for patients taking chemotherapy only.

Common side effects of Lynparza include anemia, neutropenia, leukopenia, nausea, fatigue, vomiting, nasopharyngitis, respiratory tract infection, influenza, diarrhea, arthralgia/myalgia, dysgeusia, headache, dyspepsia, decreased appetite, constipation and inflammation and stomatitis.

Severe side effects of Lynparza include development of myelodysplastic syndrome/acute myeloid leukemia and pneumonitis.