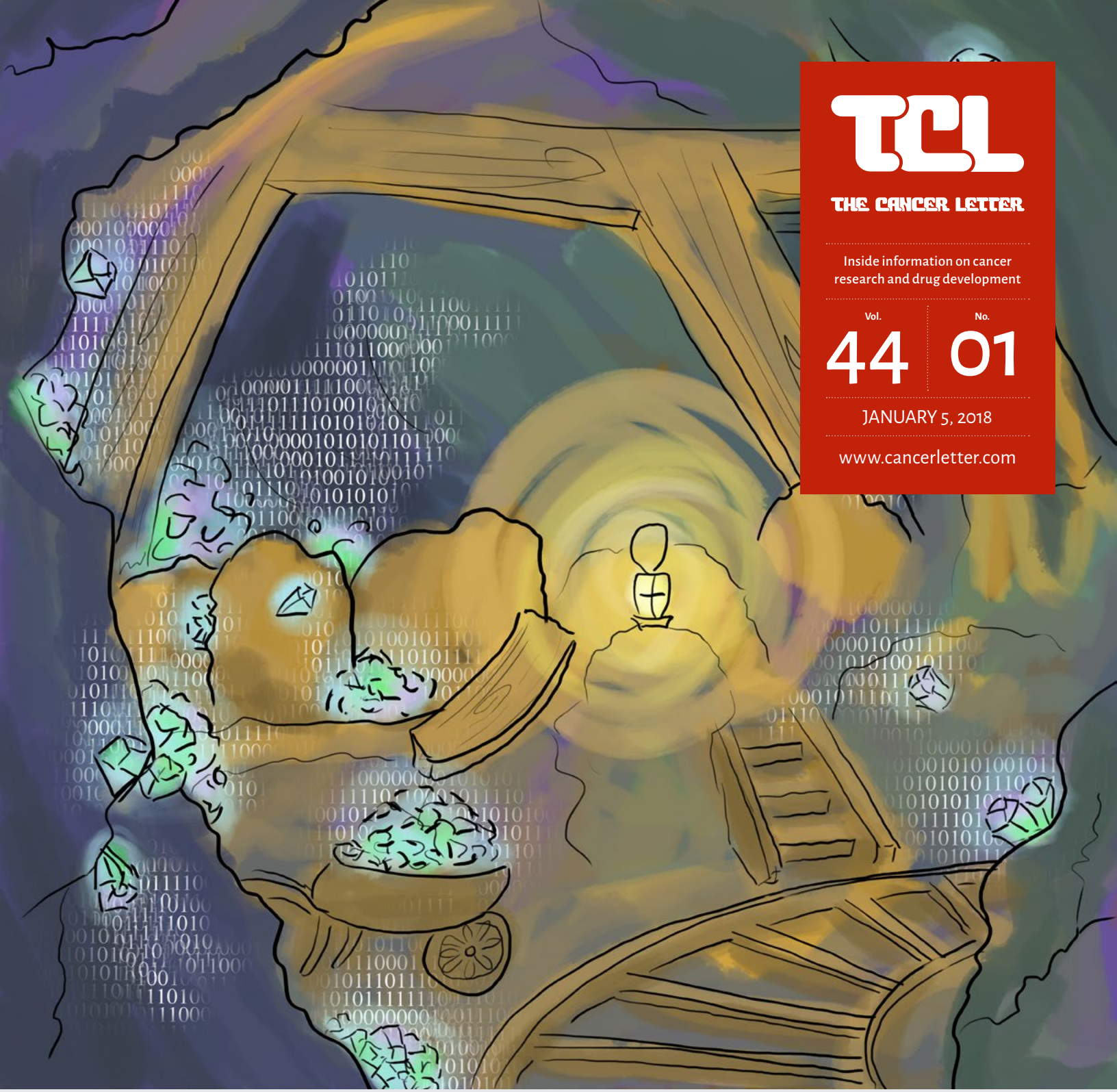

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THE CANCER LETTER
Inside information on cancer research and drug development
Vol. 44 No. 01
JANUARY 5, 2018
www.cancerletter.com

ASCO FORMS COLLABORATION WITH TWO BIG DATA FIRMS TO GROW CANCERLINQ

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Subscription $425 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

THE CANCER LETTER | JANUARY 5, 2018 | VOL 44 | ISSUE 01

Introducing the clinical section of The Cancer Letter

By Paul Goldberg

Today's issue of The Cancer Letter contains a new section devoted to clinical news.

As part of our new format, stories that have immediate clinical significance will appear in every issue, much like a sports or business section in a newspaper.

I define the word "clinical" broadly, as information you can use RIGHT NOW. This definition includes population sciences, prevention, epidemiology, trial design, electronic medical record, data mining, and privacy issues.

Here is the editorial rule of thumb: a story about NCI funding trends, or evolution of FDA approval criteria, or a 5,000-word piece about a cancer center will still go into the front section of The Cancer Letter.

However, if a story is of immediate practical importance—a drug winding toward approval, a trial you can offer to a patient, or a debate raging within a subspecialty, it goes into the clinical section. And, instead of getting clinical news monthly, you will get it every week.

Journalism is not about compilation of fact. It's about understanding what really matters. It's also about convening—understanding what people are arguing about, and making those arguments more informed, more spirited.

In this issue, we introduce a guest column titled "Trials & Tribulations." I have invited the NCTN groups, cancer centers, patient advocacy groups and NCI to provide perspective pieces, and I look forward to seeing this part of coverage evolve. If you haven't heard from me in recent weeks, let me hear from you. I am easy to reach: paul@cancerletter.com.

The Cancer Letter was founded 44 years ago by Jerry Boyd, a medical journalist and a visionary of this field. Three years later—that's 41 years ago—Jerry founded The Clinical Cancer Letter, to serve community docs, who at the time were a very different group than academics.

Four decades ago, it was possible to delineate the clinical news from the political. Today, this line is porous. This convergence of two oncologies driven by patient expectations, increasing complexity and expense of novel therapies, Big Data, emergence of immunologic and precision therapies, and increasing reliance on biomarkers. It's all one big story of systemic change, and The Cancer Letter has been on top of it.

Major cancer centers are building outreach networks into the community, getting access to patients living thousands of miles away. Some of these networks are being constructed in pursuit of academic goals. Others are built for business reasons. A new breed of cancer centers is trying to combine the best features of academia and community, and—separately—NCI is reaching out to accelerate clinical research at community clinics around the U.S. As a result, patients are being matched with treatments most likely to help them.

The Clinical Cancer Letter, which came out monthly, will now become a section in The Cancer Letter.

Here is what the change will mean to our subscribers:

- Institutional subscriptions and their prices remain unchanged.
- Individual subscribers will be prompted to switch to the combined package of The Cancer Letter and The Clinical Cancer Letter when their subscriptions come up for renewal.

By becoming a part of The Cancer Letter, The Clinical Cancer Letter will bring a new clinical focus—and a new urgency—to the combined publication.

If we do our job well—and I will see to it that we will—the new iteration of The Cancer Letter will usher in a unified oncology, where all the key players speak the same language, where silos are rare, and where all players are communicating with each other.

ASCO FORMS COLLABORATION WITH TWO BIG DATA FIRMS TO GROW CANCERLINQ

By Paul Goldberg

The American Society of Clinical Oncology has reached a deal that will allow two companies—Tempus and Precision Health AI—to curate and license the data in CancerLinQ, the professional society's venture into Big Data.

The ten-year collaboration, announced Dec. 21, gives Tempus and PH.AI access to de-identified data from over a growing database of more than a million records contained in CancerLinQ.

ASCO and its new commercial partners will continue to expand CancerLinQ and, at the same time, look for better ways to aggregate and mine the data. The data could be used in drug development as well as scientific projects and quality initiatives.

The licensing partnership will lower ASCO's spending on development of the database.

Under the agreement, Tempus will provide genomic sequencing services and structure and analyze molecular and therapeutic data to make the information accessible and useful in the clinic. Precision Health AI will focus on using artificial intelligence to define cancer datasets for precision oncology.

Together, Tempus and PH.AI will structure patient care data in CancerLinQ, which is being designed with the ultimate goals of providing quality tools, real-world data and clinical decision support. Of the 100 or so entities that have signed up to participate in CancerLinQ, about 40 institutions and practices have been activated.

This deal comes at a time when NCI Director Ned Sharpless is making it his priority to "free the data" that are siloed in electronic health records and proprietary databases (The Cancer Letter, Dec. 15). There is no legal or regulatory impetus for NCI to review ASCO's deal with the two firms, but since CancerLinQ is a major data repository that is available to academics, the institute clearly has an intellectual stake in the matter.

"Gathering and combining large, complex datasets, including clinical information and tumor genomics, is difficult, yet critically important for improving our understanding of cancer, and ultimately for making progress in cancer prevention and treatment," Sharpless said to The Cancer Letter. "Efforts at this scale are therefore exciting, and may represent great news for patients if this dataset is made publicly available to qualified investigators for academic research."

ASCO officials said that the need to put together a collaboration became apparent after five years of running CancerLinQ, as requirements for storing and curating data continued to mount.

As a non-profit, ASCO has neither the capital nor the expertise to take the project to the next level, Clifford Hudis, the professional society's CEO and

chairman of the CancerLinQ board of governors, said to The Cancer Letter.

"What we hope that the world sees in this deal is that a professional society has taken ambitious steps to build a heretofore nonexistent resource," Hudis said. "We have expended tremendous resources to get to this point, and have now identified a novel way to transparently partner with for-profit entities to bring expertise to allow us to deliver faster on our mission.

"That really is why we are doing this. It is not a sale; there is nothing being sold. It is a licensing arrangement. But our number-one aim is to enable our members to deliver higher quality care more broadly and faster than before."

A conversation with Hudis appears on page 8.

The terms of the deal were not disclosed, and ASCO hasn't released its budget numbers for CancerLinQ. When the program was announced in 2013, Hudis, who at the time was the ASCO president, said that it would take $80 million to fund CancerLinQ through the first five years (The Cancer Letter, Dec. 3, 2013).

At this stage, five years later, it's apparent that hundreds of millions of dollars will be required to cleanse, structure and expand the data to a level where it could enhance quality and provide real-world evidence and patient outcomes for researchers and pharmaceutical companies, Hudis said.

Under the licensing arrangement, CancerLinQ will remain a non-profit and will still be responsible for data integration and provision of tools and reports to participating oncologists and cancer care sites, ASCO said.

Academic and commercial projects going through the CancerLinQ Discovery, a service that allows subscribers to submit requests for customized sets of anonymized and statistically de-identified real-world cancer care data, will be handled differently, ASCO officials said. The CancerLinQ Discovery Research and Publications Committee will continue to review requests for access to data from non-commercial users, such as academic researchers. Tempus and PH.AI customers may also avail themselves of Research and Publications Committee review if they so choose.

In situations where Tempus and PH.AI enhance the CancerLinQ data through correlation with other datasets, the resulting datasets may, in some cases, be made available to CancerLinQ users, ASCO officials said.

"I've been in technology for 20 years, building companies that all kind of do the same thing. We structure unstructured messy data and try to bring technology to industries that have not had a lot of technology, whether that's printing or logistics or manufacturing or local commerce, and I've never seen anything like what's happening in health care, and in particular, in cancer care," Eric Lefkofsky, co-founder and CEO of Tempus, said to The Cancer Letter.

"You have these massive technology paradigm shifts hitting oncologists and pathologists and radiologists and surgeons all at one time," Lefkofsky said. "One is the revolution in our ability to collect and analyze genomic and transcriptomic and proteomic data—in other words, molecular data—at very low prices relative to what they were just 10 years.

"There's been a million-fold reduction in the cost of generating genomic data in about 10 years, which is just staggering. At the same time, you have equal advancements in machine learning and artificial intelligence, especially on the image recognition side of this, impacting our ability to read pathology slides or read radiology scans and draw important clinical distinctions.

"So, you have these two incredible technology movements hitting physicians that are treating cancer patients all at one time, and I do think it's massive, and I think organizations like ASCO and their commitment to CancerLinQ and their commitment to getting ahead of this, is really extraordinary. I think it's a model for how all associations should be thinking about how to have an impact in their respective diseases."

A conversation with Lefkofsky, who is also a co-founder and chairman of Groupon, appears on page 16.

"We are developing an innovative AI platform for the management, delivery and use of clinical data. Our experienced team of health care data and technology professionals focus on developing artificial Intelligence and machine learning-driven solutions for a range of oncology stakeholders," Romesh Wadhwani, chairman of Precision Health AI, said in a statement. "Applying our technology solution to de-identified CancerLinQ data will help the broader community to accelerate research and the development and administration of new therapies."

Even with this deal, CancerLinQ will not break into the black, Hudis said.

"Our goal is to get CancerLinQ to break even," he said. "We're not quite there, but we're closer and we're sustainably close enough.

"It'll become a modest enough loss that we could afford to do it, if it's delivering value for a long time."

Matthew Bin Han Ong contributed to this story.

Q & A

Hudis spoke with
Paul Goldberg, editor and
publisher of The Cancer Letter.

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CONVERSATION WITH THE CANCER LETTER

Hudis: ASCO needed collaborators to help CancerLinQ deliver faster on its mission

Clifford Hudis
CEO of the American Society of Clinical Oncology and chairman of the CancerLinQ board of governors

> We are a non-profit, a 501(c)(3), we have a societal mission, and we could neither afford to develop this rapidly on our own, nor could we obtain all of the technical skills to accomplish our vision quickly and efficiently internally. That's why we need collaborators.

Paul Goldberg: Thanks for agreeing to make an effort to get this through my thick skull.

Clifford Hudis: It's kind of you and overly harsh. But anyway, I am happy to talk today.

How would you summarize what is happening? Is this a sale? Is this a licensure?

CH: This is a licensure and a strategic collaboration. This leverages the expertise of several organizations to allow us to deliver real value to our members and subscribers faster than we would have been able to otherwise.

First of all, who is involved?

CH: There are two parties for this. One is Tempus, a technology company that provides genomic sequencing services and structures and analyzes molecular and therapeutic data. It is based in Chicago and run by Eric Lefkofsky [founder and CEO], who is one of the founders of Groupon.

And the other is Precision Health AI, which was founded by Romesh Wadhwani.

They each have expertise and experience in complementary domains, but they came together to talk about licensing access to our data.

And that's what this deal is.

In the simplest terms, this deal consists of three things:

Number one is that our collaborators gain license to access our data for a period of time. We obtain a revenue stream, which defrays a substantial—but not total—cost of CancerLinQ.

And they also bring curation expertise, and that's something that all real-world data needs. Plus, everything they do to curate the data for any purpose also simultaneously feeds back to enrich and improve the CancerLinQ data.

Finally, they bring exceptional technical expertise, so they can help us deliver vital offerings back to our members faster than we were going to without them.

Can you give me the numbers?

CH: Which part of the numbers?

We could start with how much ASCO has invested in CancerLinQ, and how much it costs, to maintain it?

CH: ASCO has made a steady and growing investment in CancerLinQ, because we truly believe in the vision that better data can lead us to better cancer care.

This investment includes not only revenue, but also the intellectual resources of most parts of ASCO so it is hard to fully quantify. Even with this deal, we do not foresee a positive operating margin from CancerLinQ, but if its services enables improved care, then it will be a success for our members.

How do you report the CancerLinQ expenditures?

CH: There is an annual budget for CancerLinQ, but one of the nuances of CancerLinQ is, it is a wholly-owned non-profit LLC that's completely contained within ASCO, so it's not a separate business financially.

It's a wholly owned enterprise within ASCO, so ASCO's budget, it contains CancerLinQ. And there are some shared services, so it's always a little tricky to get very specific about CancerLinQ revenue and expense.

It's not a line item?

CH: It's many line items, that's right.

One of the problems or challenges we have faced, of course, is that the entire operating expense for CancerLinQ significantly exceeded its revenue, and it has had to be backstopped by ASCO funding.

We are cutting the deficit from CancerLinQ through this transaction. Our goal is to get CancerLinQ to break even.

We're not quite there, but we're closer and we're sustainably close enough. It'll become a modest enough loss that we could afford to do it, if it's delivering value for a long time.

How many people do you have working on CancerLinQ?

CH: I think it's about 55 right now. It may go up this year of the transition.

Do you have any estimates of what it costs to deliver on the promise of CancerLinQ—what the total investment level might need to be?

CH: My guess is over the long run it's hundreds of millions of dollars if not

even more. By the way, if you think about what drug developments numbers are, what I just said isn't so shocking, is it?

No.

CH: Right. It's not feasible for a nonprofit.

What about the deal with SAP? (The Cancer Letter, Jan. 23, 2015)

CH: We have a contract with SAP, where we are the customer.

They provide technical support, warehousing, and additional services that are not directly or immediately affected by what we're doing here.

What is the data they're licensing from you?

CH: Let's just back up a half step.

The way that the CancerLinQ works is distinct from the registries that some other professional societies have created.

I actually think one of the goals of our discussion should be to clarify the distinction. These registries are, generally speaking, purpose-built and used to answer a specific question. It's easiest to describe with an example.

Imagine that the FDA needs surveillance on outcomes with an implanted device. Maybe the relevant society would develop and run a registry and their members would record all the device implants along with certain relevant fields. Then, when you're done, you have a pretty good snapshot of what's going on in the world with those things.

And that's something we're used to. However, CancerLinQ is very different.

It represents a download of the totality of all of the recorded data in the electronic records of participating doctors and practices and hospitals. In that regard, it's deeper and richer than any other focused dataset, but it's also less structured and it's often less complete. And its fitness to answer any specific question is variable. The data is sometimes there, but not in the same places in every chart.

Again, it's easier to describe with specifics than generalities. You could imagine that for one patient, there is a staged description of their cancer, T2, N1, and M0 tumor in a data field labeled TNM and that's structured. You can imagine the very next patient had their procedure done outside of a health system, and a physician had a paper note in front of him and it's literally written into a progress mode with the TNM in it.

So, while both are functional for the patient and doctor and contain that information, in one situation, a computer program can recognize the labeled field and say, "That's T, that's N, and that's M." But in the next, it requires either a real or virtual reader to parse it out of the written notes.

So that's curation. And the only way that you can take existing records like we have and reliably find the data outside of the structured fields is to curate them.

And that's expensive.

CH: Yes, and we've been doing it already. We've learned a lot and we know what it takes. Our new collaborators bring in complementary curation skills to the mix here for us. And as one example, if you go back to Groupon before, which is what Eric founded, you know Tempus obviously has deep experience looking at data inside and outside of medicine.

On the other hand, Romesh has tremendous experience with medical data and finding the relevant components of it, and also with importing external data to enrich what we have. So, we're going to be on a journey together.

We're going to be developing natural language processing, we're going to be accelerating curation, and we're going to be generating new and better data, so our users that will have a richer data resource than before.

And what they're going to be getting is access, ultimately, to the de-identified data, and they're going to be curating it, and sharing that with us while they're able to commercialize the process.

How much data is it and what kind of data is it? How many patients, how many practices?

CH: We have more than 100 distinct entities already signed up for CancerLinQ with more to follow.

Of those who are signed up, we have been able to onboard around 40. Now, I want to pause here, because it's not that we're not trying, but one of the ambitions that we had was to serve all members, and one of the consequences of that ambition is we never said we would only use name brand medical records.

We said we'll take any. And we didn't say we would inspect your record and only take it if it's above a certain threshold for completeness or quality. Adding even more complexity is the fact that each installation of each electronic record system can be unique to some degree. They are often customized, and they then get upgraded at varying rates.

We have to constantly adjust our intake system for each version and each installation of each medical record. The data we bring in is widely dispersed, it has to be homogenized and normalized, which is a CancerLinQ function now, and then it goes into a database. Then we have a series of databases that are increasingly clean and increasingly de-identified leading to the ones that our partners can access.

I see. But what are the numbers? Is it 1,000 patients, 500,000 patients?

CH: So, of the roughly 100-plus entities that have signed on, we have about 40 that are onboarded. We have about one million cancer patient records right now from about 600,000 individuals.

One of the wrinkles is, we've got, I think, it's just shy of 3 million patients potentially right now, and rising.

On the other hand, they don't all have cancer. For example, some of them are hematology patients or even general medicine patients that might be in a practice for various reasons. But when you get down to diagnosed cancer patients, we can analyze right now, the number is about 600,000 patients.

So, it's 600,000 patients?

CH: Yes. But this is the beginning. We've been onboarding them for a year-and-a-half, and we have more than half of our potential patients yet to be onboarded, and we have steady growth in our market penetration right now. So, there's a lot more out there ahead of us than behind us.

So, ASCO is continuing to do this?

CH: Oh yeah.

And you will continue, even after this licensure deal?

CH: Absolutely. There are two aspects of it.

We will always need to be updating this because, of course, treatment changes and modernizes, and we always will need to get current data. The second issue is that the real reason we did this in the first place and what this deal allows us to focus on even more is to support our members delivering high quality care.

That means tools and applications that run against their records so that they can improve their care. It also means that we're going to be hooked up to the ones we have and hooking up more so that we can learn from more and distribute more knowledge and tools.

What about the rapid learning system? Is that still going to happen?

CH: Well, that was the beginning of all of it. You'll remember the discussion back at the beginning of the decade. And on an aspirational level, I would say that's still very much out there for us.

I see. How does monetizing look in this case? What is the structure?

CH: So, again, we are a non-profit, a 501(c)(3), we have a societal mission, and we could neither afford to develop this rapidly on our own, nor could we obtain all of the technical skills to accomplish our vision quickly and efficiently internally. That's why we need collaborators.

We needed to find mission-aligned or compatible entities who saw a way forward to a successful business model so that they'd be willing to invest and would be able to support us in delivering on our mission.

It was an interesting journey to find the right structure. What they're going to do, and we certainly will support them, is go out to pharma, payers and other for-profit entities, and they will be able to sell them analytics running off of curated, enriched and de-identified data. They see a business model that is obviously profitable enough to justify their long-term investment.

Can you think of specific questions that they might be able to answer?

CH: Well, they'll be able to answer questions about real-world use and outcomes for treatments.

Any other clinical questions? Like how are people using drug A?

CH: That's what I mean. So, a typical example would be you take some modern therapy, newly approved in phase III, where a group of very qualified patients have been used in a study to prove their treatment has the given effect.

And that provides the label. It is typical to find in the real world that the patients who get treated of course don't completely match that pristine cohort in both specific or general ways.

Patients in the real world have hypertension, diabetes, and other medical

problems that may have been exclusion criteria in the formal studies.

As a consequence, it is common to find that the use of the drug in terms of, let's say, duration and its benefits, is modulated in the real world. That's the kind of information that we will get here. That's a typical, real example.

What about a question like, what is the prevalence of a specific condition?

CH: Sure. Natural history, outcomes and more. Remember, at the same time, some of these are the kinds of questions that would be of great interest to academic researchers and wouldn't be equally so to for-profit businesses.

And ASCO continues, therefore, to provide access to our ever-improving database for the cancer community. That's one of the direct benefits of the deal.

And you continue to co-own? Do they own it? Do they license?

CH: They license. There is no sale of anything here. They are paying us an annual fee, and you could really consider that fee as dollars and curated records. And based on that, they are able to license the data and sell it to the markets that are theirs.

And how long is this for?

CH: Well, I hope for a long time. It's a ten-year deal in structure.

There is an offshoot of CancerLinQ. CancerLinQ Discovery I believe it's called. Is that what is being licensed?

CH: CancerLinQ Discovery is our offering to the academic community and others for research. And that's one of the beneficiaries of this deal, because the data in CancerLinQ Discovery will be more rapidly improved from their curation.

The CancerLinQ Discovery and research and publications committee, which we call R and P, that will continue to function reviewing all requests to access data from noncommercial customers. So, all the usual academic researchers who come through CancerLinQ will follow the data access policy, and they will go through R and P review, and they will gain access to CancerLinQ that way.

They (Tempus and Precision Health AI) will, you know, be able to pull into their data whatever CancerLinQ data is necessary for them to address their commercial needs. But de-identified. This is really important. Nothing identified ever goes through.

The part that I never understood is the value of this. Correct me if I'm wrong—I'm probably wrong—does the data come from community practices, as opposed to academic institutions?

CH: Not as opposed to, in addition to. That's actually what makes this deal valuable, I think. It is not a selected cohort of people who go to referral centers.

Nor is it only the people who go to private practices. It is the full range of government-supported, low-income centers, to high end and socio-economic settings. It is small to large, it is private practices through most highly respected academic centers in the country. It is a full range of practices and settings.

That's good to know. But of those 600,000, is there an overall balance in this picture?

CH: Well, that's a really interesting point. To make this data most valuable, one of the places where we will be collaborating with them on an ongoing basis is to make sure that the curation is balanced across these different types of practice settings, as well as different diseases and demographics so that, over time, the data set is broadly reflective of all these elements.

So, you have to really grow the dataset to be reflective of what's actually going on?

CH: Well, it's not just grow the datasets, which we do have to do, but we also have to be thoughtful about the priority we place upon curation of different subsets.

For example, if we only curated data from a tertiary referral center, our improved offerings of CancerLinQ Discovery would be skewed. Instead we have to make an effort to make sure that as we curate, that we're curating from all of the practice settings so that the data that researchers and our partners have is truly real world and not a skewed subset.

Do you see a possibility of using this for drug approvals, running clinical trials?

CH: I think it will contribute. I also think we have to be humble about real-world data for lots of well reported reasons. Let's just talk about this for a couple of minutes, and you start to see how this fits into the broader canvas.

In the past, drugs would get approved and labeled and you've covered this many times in the last few years under different stories. It would get approved, and then they would get used by the community and they would typically get used off-label.

And that's because there was little incentive for companies to go and file for a label in every possible indication. Also, there was an expectation after the FDA said a drug was both safe and effective, that the community would identify all of the uses, continue to adjust it.

After all, the FDA did not, in a restricted way, prescribe the practice of medicine. What they did was enable it. And this is an important difference there, because this comes up all the time when we talk about high drug prices and the role of the FDA.

Their job was never to control the practice of medicine exactly, it was to make sure that drugs are safe and effective when they're put into the market, and allow the marketplace to continue to refine their use. This is our history.

And to prove it, you can go back and look at any of a dozen chemotherapy drugs from the 60s, 70s, and 80s, and then look at where they're used first at the label, and you'll remember there wasn't really controversy about that.

It was expected. As drugs became much more expensive in the last years, many third parties began to restrict use in various ways to the label. And from a certain perspective, this was not the intention of the FDA label. It wasn't established to restrict access or use, but it was applied that way by a third party, not by the FDA, but by the third-party payers.

So now we go in the modern era, and this will get us to CancerLinQ, but let's just think for a second about what happened with ASCO's TAPUR study. You've got next generation sequencing taking place all over, and this is even before the decision on the Foundation Medicine test last week.

And now you've got docs who have the following situation: they have a patient with a specific histology. In that histology, they have a specific genomic alteration, they have a reasonable, theoretical argument to give a targeted drug to that patient. That targeted drug is on the market because it's FDA-approved for a different disease, and they yet find that they can't do it, because now the label is being used to restrict your access by the payer.

The TAPUR study matches those patients, allows us to learn whether there's something there or not. And in the latter case, if we treat a small number of patients with a histology and mutation or alteration and a targeted therapy and there's no response, we can reasonably conclude that even though it made good sense, that's not an effective therapy. And that's helpful to patients, the community and the industry to know that.

The flip side is, we might see some evidence of activity, and that evidence of activity might lead to either a bigger, purpose-built study in some cases because the sponsor could build on the fact that there's a bit of a promise already, there's some evidence of activity. Or it might lead to actual label extension in some cases. Maybe the agency would accept the TAPUR data which is closer to real world because the eligibility criteria and the whole way we run TAPUR is closer to everyday practice.

So, now that brings me back full circle to CancerLinQ. We have real-world patient data in there, some of which might be convincing at least that there is the possibility of activity for specific drugs and matches.

Maybe that's just enough to get a study launched, maybe in some cases it'd be more convincing than that. And then the other side is, the CancerLinQ data may provide for modern synthetic control arms, which would allow companies in some cases to either model more efficient studies, or even use the control data from CancerLinQ to support label extensions. I think this is a new world, and we'll have to see how good the data is and whether it can be used for any of these purposes.

Maybe the question is how does this loop into CancerLinQ ... Let me rephrase that. How does next-gen sequencing loop into CancerLinQ?

CH: One of the challenges we have, frankly, is only certain patients under certain conditions are getting sequencing.

Only some of that data is necessarily being recorded or fully recorded in the charts the docs have. And so, it is not the case that CancerLinQ is necessarily a genomic data set. It's just the recorded data as it exists for individual patients.

To the degree that some patients will in decent numbers have accurately recorded, well done genomics and to the degree that they can be subset-ted and identified and studied, yes, it'll be another contributor.
But, this brings me back to where I started at the beginning. One of the challenges of that it is a full data set versus a registry. It is "take it as you find it" data.

It would be more useful as a way to find signals of something you might want to try?

CH: Absolutely. Right, I think so. And also, there are so many things we don't know. It'll be a way of identifying natural history in the real world when there are other diseases present. It'll be a way of identifying the size of populations, which are increasingly segmented by genomic and other factors.

It'll be a way of identifying geographic distribution and access to patients for planning a research study. So, this data is going to have value in many ways, but I think that value may be in some cases different from what many traditional researchers imagined. It's not a replacement for prospective planned, well done research. It isn't. And we would not be doing ourselves or the community any favor by misunderstanding it that way.

One can easily imagine that it will provide insights that would allow us to develop more efficient prospective studies. It'll contribute to a world where we don't have to do quite as many studies that are dead ends.

Which of the three parties is responsible for developing clinical decision support? Which of the three parties is developing real world evidence capabilities?

CH: All three parties will be working, both collaboratively and in parallel, to develop clinical decision support tools and to evolve the clinical and scientific utility of real-world evidence. The primary role differentiation relates to commercial activities which are the exclusive responsibility of Tempus Labs and Precision HealthAI.

ASCO's commercial partners are using CancerLinQ data to build enhanced capabilities based on CancerLinQ. Is there any aspect of this endeavor that only ASCO is doing? What is ASCO's role in CancerLinQ now, as a result of this deal?

CH: CancerLinQ's prominent role will continue in a fashion consistent with the founding principles of the initiative. CancerLinQ will continue to:

- Maintain the relationship with the participating oncology care teams.
- Maintain custodial control and responsibility for all personally identifiable data.
- Manage the outreach to and ongoing relationship with cancer care centers.
- Manage the technical integration with subscribers' EHR systems.
- Manage data ingestion and normalization.
- Offer a de-identified data resource for academic researchers.
- Manage the various committees of patients and clinicians who provide guidance to CancerLinQ.
- Manage the Oncology Leadership Council, that growing body of sister societies and regulatory agencies that provide guidance to CancerLinQ.

How do revenues get to ASCO to get CancerLinQ to revenue neutrality and how soon will this happen?

CH: CancerLinQ will receive an annual royalty in exchange for a license to utilize de-identified clinical data. This licensing fee will make up the majority of CancerLinQ's operating funds beginning in 2018.

How effectively are third-party payers using real world evidence now? How can real world evidence be used to inform their decisions—and do you see this actually happening?

CH: At present, claims data continues to be the predominant form of data used by third-party payers. However, we are already seeing a gradual evolution in their utilization of real-world evidence, just as we have seen at the Food and Drug Administration and in the bio-pharmaceutical community.

Is there anything we've missed? Anything you'd like to add?

CH: I hope that the world sees in this deal that a professional society has taken ambitious steps to build a previously nonexistent resource.

We have expended tremendous resources to get to this point, and we have now identified a novel way to transparently partner with for-profit entities to bring expertise to allow us to deliver faster on our mission.

That really is why we're doing this. We are of course sensitive to possible misperceptions about this deal. It is not a sale; there is nothing being sold. It is a licensing arrangement, it has a term, we will see how it goes.

But our number-one aim is to enable our members to deliver higher-quality care more broadly and faster than before.

Q & A

Lefkofsky spoke with Paul Goldberg, editor and publisher of The Cancer Letter.

THE CANCER LETTER | JANUARY 5, 2018 | VOL 44 | ISSUE 01

CONVERSATION WITH THE CANCER LETTER

Lefkofsky: CancerLinQ has value in ushering in an era of precision medicine

> This data has some commercial applicability today. But the real value in this data is in how do you build much larger, much more comprehensive datasets that actually can be used to usher in an era of precision medicine.

Eric Lefkofsky
Co-founder and CEO of Tempus

Paul Goldberg: How is the CancerLinQ deal structured? What is happening with this?

Eric Lefkofsky: As you know, ASCO formed CancerLinQ some time ago with ambition of trying to aggregate data, the real raw-source data, meaning patient records, from across a broad part of the oncology community. The goal being, if they could get these data sets that were locked inside electronic medical record systems and electronic hospital records systems, they could look for patterns that were clinically relevant, look for patterns that would improve quality of care, and look for patterns that would ultimately lead to new research.

So, they established CancerLinQ, and they were getting all this source data, which was really amazing—their penetration of the market has been extraordinary—but as the data began to accumulate, they found themselves with the challenge of what do we do with all this data?

How do we structure all this unstructured data? And the data was actually coming in so fast that I think it was a bit overwhelming. So they began to search for partners who could help them structure this data. And at the same time they began to look for partners to structure the data, it also became apparent that once the data was structured there would be multiple avenues that it could be put to use to help make it useful. Obviously, one of them is how do you improve decision support for clinicians and how do you improve research?

But there are other implications, including how do you get some of the insights from this data into the hands of biotech companies and pharmaceutical companies to make better drugs? How do you get this data into the hands of people who run clinical trials so they can run more efficient clinical trials? How do you get this data into the hands of people who make reimbursement decisions to determine which drugs to pay for?

So, they began a journey to look at a variety of companies that might help them, not only structure this data, but also help them bring it to practical use. They met with a bunch of companies, who obviously were interested, and at the end of that process they ended up selecting Tempus and a company called Precision Health AI, as their two partners to help them both structure and bring the data to market.

In terms of Precision Health AI, how does that work, in terms of your relationship with them?

EL: We are two separate companies. We actually met during this process. We were both independently working with CancerLinQ. We were both interested in helping them with this data, and we decided at some point several months ago that instead of going at it independently, we would go at it collectively, and we would both approach CancerLinQ and ASCO and say "we want to work together with you collaboratively."

We are still two separate companies, but right now we believe it's better to have two separate companies than one company curating and abstracting and cleansing the data and improving its use. So, they ultimately agreed with that approach and selected us as their partner.

How far is this from being monetized?

EL: CancerLinQ announced some time ago that they already have a collaboration with AstraZeneca. They have other collaborations that they have announced as well. So, it's less about how the data is monetized... I can only tell you our approach; right?

That's what I was asking for.

EL: This gets a bit into Tempus's business model and at least how we view the world. This data has some commercial applicability today. But the real value in this data is in how do you build much larger, much more comprehensive datasets that actually can be used to usher in an era of precision medicine.

The data is interesting today, it absolutely has some practical application today. But these kinds of datasets at scale have yet to be used to truly impact care in the ways we all envision. What you are really thinking about when you are talking about structuring clinical data is how do you build a sustainable model that's going to allow you to structure this data and ultimately use this data.

It's less about how do I make money in the short term. It's more about how do I create sustainability.

And I will tell you what I mean by that: twenty years ago, when we migrated to electronic medical record systems (big EHR and EMR systems) there was a movement to do that very quickly, in large part based on reimbursement, and what happened in the creation of

these systems is that we basically took a lot of the complexity—the key phenotypic, therapeutic and outcome response data—and we just left it to the side, essentially in free text and images.

We left it inside physician progress notes, left it inside pathology reports, left it inside radiology reports, or it sat inside scans, or it sat inside pathology slides. And nobody tried to structure that data. It was just too big of a process and too expensive.

And so here we are today, with 15 million people with cancer in North America and this enormous amount of data that's unstructured. And so what CancerLinQ set out to do and what Tempus has set out to do is to create a model that would allow you to pool data from the people who have it and begin to structure all that unstructured data in a way that would allow you to look for clinically relevant patterns or patterns that could lead to better research.

There is a cost to basically structure that data, depending on the patient record, whether it costs you $25 or $50 or $100 or $250, whatever the number is. And since there is a cost to structuring that patient's data, you will ultimately want to create a sustainable model that allows you to do that not just for 1,000 patients, but for 10 million patients.

To me, this is more about how do you get that data structured at a large enough scale that you can get the various constituents inside the healthcare industry interested in helping you build something that's sustainable.

And that's the part of the journey we are all on right now; which is, okay, we need to have a million patients, or two million patients or five million patients with structured clinical data in order for people within the industry to say, "All right, I want some of that de-identified data for this purpose or some of that de-identified data for that purpose, and I am willing to pay you and help you create a data ecosystem that can scale."

I think when we talk about commercialization or monetizing the data, and it's still early days. We are really just starting down the journey to make these datasets valuable, and just beginning to have the earliest conversations with people to say "how do we create a new model where data flows freely, and it's adding real value".

How much do you think you need to be investing in this right now?

EL: I can only speak for Tempus—PH.AI, of course, has made its own investments that are significant in this space—but at Tempus, we put $130 million into Tempus, and we expect to put hundreds of millions more over time.

This is a significant endeavor for us. And it's long-term, and one that we believe is invaluable, not just based on the impact it has on patients, but also it has value in the market, and in ushering in an era of precision medicine.

The $130 million is all of Tempus; it's not just CancerLinQ?

EL: It's Tempus and, as I said, Precision Health has invested lots of money as well. I don't know the exact amount, but they have invested significant money in the formation and capitalization of PH.AI.

These are two formidable, well-capitalized businesses that are coming together as part of this collaboration, trying to make this data more valuable and improve patient outcomes.

Are you and PH.AI doing the same things or different things? Are you complementing each other?

EL: I thing we complement each other. They are more focused on machine learning and analyzing large datasets and combining these datasets with other datasets to look for patterns that are interesting.

Our focus on this has been more on combining clinical data with molecular data. We have a very strong molecular data orientation, which is why we built a lab to sequence patients. We believe that the patterns that are most interesting in cancer in the short-term are based on combinations of clinical and molecular data, predominantly, how do you amass large datasets to answer the following questions: who are these patients, how are they being treated, how are they responding to treatment, and what's their molecular profile and composition, and can we see something in that molecular profile that we think is indicative of how a patient might respond to a given therapy.

That's been our mission since we launched Tempus.

But as far as, do you foresee a situation where you're sitting there and reading or having people reading records—just humans?

EL: We do that today. We have a significant operation today; we have very large teams structuring clinical data today, even unrelated to CancerLinQ, and we use a combination of optical character recognition technology and natural language processing, and humans. We have something like 120 people today abstracting and curating clinical records, and that team grows by something on the order of about 25 to 30 a month, so it's a rapidly scaling team that curates and abstracts clinical records for cancer patients.

I see. It sounds like such an enormous thing. It's probably bigger than all of ASCO in terms of the amounts of money that needs to be committed to this.

EL: You know, it's not small.

You know, it's sort of interesting how it grew as an undertaking for ASCO. It's probably larger than the organization itself, to do it right.

EL: ASCO is a very large organization, and you have to talk to, obviously, Cliff and Kevin [Fitzpatrick, CancerLinQ CEO] about that, but I do think—I can speak to the comment you just made. I've been in technology for 20 years, building companies that all kind of do the same thing.

We structure unstructured messy data and try to bring technology to industries that have not had a lot of technology, whether that's printing or logistics or manufacturing or local commerce, and I've never seen anything like what's happening in health care, and in particular, in cancer care.

You have these massive technology paradigm shifts hitting oncologists and pathologists and radiologists and surgeons all at one time. One is the revolution in our ability to collect and analyze genomic and transcriptomic and proteomic data—in other words, molecular data—at very low prices relative to what they were just 10 years.

There's been a million-fold reduction in the cost of generating genomic data in about 10 years, which is just staggering. At the same time, you have equal advancements in machine learning and artificial intelligence, especially on the image recognition side of this, impacting our ability to read pathology slides or read radiology scans and draw important clinical distinctions.

So, you have these two incredible technology movements hitting physicians that are treating cancer patients all at one time, and I do think it's massive, and I think organizations like ASCO and their commitment to CancerLinQ and their commitment to getting ahead of this, is really extraordinary. I think it's a model for how all associations should be thinking about how to have an impact in their respective diseases.

Is the decision support system still a possibility or was that something that was science fiction, based on CancerLinQ?

EL: I think when you have datasets that are large—at some point, we'd have to figure out and I mean, we can log in to WebEx as long as it's confidential, and we can show you our system today, which might make sense for five minutes at some point.

I'd love to do that in a different story. I can also hop on a plane and come see you.

EL: When you see what we built, unrelated to CancerLinQ, I think it will make more sense. We have agreements now with the majority of NCI cancer centers in North America and a significant and growing percentage of the market outside NCI cancer centers. We've built, in a very short period of time, a large footprint where we're both sequencing for oncologists and producing genomic data and also helping them analyze their data and make sense of it.

We attempt to use that data today to help answer a series of questions, again, largely from a molecular lens, because we tend to be more focused there. But it is real-time decision support, so you've got a pancreatic patient and they failed first-line therapy—and you're considering between a second-line therapy or maybe you're considering between Folfirinox and gemcitabine/Abraxane, or whatever the chemotherapy options are—and if we can see that if the particular molecular profile of that patient, maybe the patient has a CDKN2A mutation or some other mutation that appears based on the totality of evidence we've been able to collect, to be driving better responses for one chemotherapy vs. another or a targeted therapy vs. chemotherapy, or radiotherapy vs. chemotherapy—that's data that you as a physician want to have.

Because, ultimately, there are times when the guidelines allow you as an oncologist to consider multiple therapies. There is no clear path that's going to lead to a good outcome, so you as a doctor want to have all the data that you can have at your fingertips. What people like CancerLinQ are trying to

do and what Tempus is trying to do and what PHI is trying to do, is get that data and put it in one place—in hands of people that are making those types of decisions.

I think we're actually, in cancer, much closer to real-time true decision support than people think. I don't think it's a decade away; I think you're going to see really significant changes in the field in the next couple of years.

Can you think of other research questions that you will be able to answer with CancerLinQ that you might not be able to answer quite as quickly, or at all, right now?

EL: Yes. What ends up happening is, let's just think about immunotherapy for a minute. There are roughly 8,000 clinical trials in North America, at least there were the last time I looked at the data. Well over 1,000 of those trials were immunotherapy-based, and so, you have an enormous number of trials and you have an enormous amount of oncologists today that are looking at immunotherapy as an option, especially for metastatic patients or late-stage patients or high mortality rate patients.

There's very little data on whether or not some of these known therapies are actually producing durable responses or non-responses. We talk all the time about MSI status or tumor mutational burden or mismatch repair genes that may be mutated or immune infiltration or HLA typing, or any one of these different markers that seem to be leading to a particular response.

The data is very sparse, so when somebody like CancerLinQ can aggregate this data from the field and start to collect insights on which patients have taken a checkpoint inhibitor or some other immunotherapy drug and had a positive response, or which patients haven't. That information is super powerful in that it can be a really big flashlight leading the way not just to new trials, but also to a refinement of existing practice.

I think you're going to see, as we start to cleanse and structure data at really unparalleled rates, because remember what's also really interesting here is the technology backdrop that's allowing us to scale. We talked about imaging and genomics, but there's an equally powerful technology paradigm shift in our ability to store data, to structure data.

These tools are really just a few years old, where we now can use natural language processing and we can use other techniques to structure data. You're going to have these massive new datasets that are going to arrive that are providing incredible insight that there just not cost-effective to build even ten years ago.

Maybe it cost $50 to abstract a record today whereas it would've cost you $500 or $5,000 five or 10 years ago. It just opens up the door to new possibilities.

AN APPRECIATION

Jimmie Holland, founder of psycho-oncology, dies at 89

By William Breitbart

Jimmie C. Holland, internationally recognized as the founder of the field of psycho-oncology, died suddenly on Dec. 24, 2017, at the age of 89.

Dr. Holland, who was affectionately known by her first name "Jimmie", had a profound global influence on cancer care and research; highlighting the critical importance of "whole person cancer care", through her groundbreaking work on quality of life, screening for distress, and the psychological, social and emotional well being of cancer patients at all stages of diagnosis, treatment and survivorship.

Over a 40 year career at Memorial Sloan Kettering Cancer Center, Jimmie created and nurtured the field of psycho-oncology, established its clinical practice, advanced its clinical research agenda, and through her pioneering efforts, launched the careers of the leaders of a national and worldwide field who mourn her passing and continue to

work in what has become a shared mission to emphasize "Care" in cancer care.

Dr. Holland was the attending psychiatrist and the Wayne E. Chapman Chair at Memorial Sloan-Kettering Cancer Center and professor of psychiatry, Weill Medical College of Cornell University in New York. In 1977, Jimmie was appointed chief of the Psychiatry Service in the Department of Neurology at MSK, by Jerome Posner, MD, then chairman of neurology at MSK.

The Psychiatry Service at MSK was the first such clinical, research and training service established in any cancer center in the world. In 1996, Dr. Holland was named the inaugural chairwoman of the Department of Psychiatry and Behavioral Sciences at Memorial Sloan Kettering Cancer Center; again the first such department created in any cancer center in the U.S. and the world.

Dr. Holland founded the American Psychosocial Oncology Society in 1986, and founded the International Psycho-oncology Society (IPOS) in 1984. Over 25 years ago, Jimmie founded and co-edited, the international journal *Psycho-Oncology*.

Dr. Holland edited the first major textbooks of Psycho-oncology and recently edited the 3rd edition of the textbook "Psycho-oncology" in 2015. Jimmie co-wrote two well received books for the public: "The Human Side of Cancer", and "Lighter as We Go: Virtues, Character Strengths, and Aging"; the latter reflecting her interests in Geriatric Oncology as she approached her 90th birthday.

Dr. Holland was born in the small farming community of Nevada, Texas in 1928. She credits the local family physician in that community with her interest in medicine and caring for those who were suffering. Jimmie was 1 of only 3 women in her class at Baylor College of Medicine.

In 1956 Jimmie married the renowned oncology pioneer James Holland, MD, who was then chief of medicine at Roswell Park in Buffalo. Jimmie recently described her early collaborations with James in a video interview with IPOS. "I started the *Special Medical Clinic* to provide psychiatric care to cancer patients. They didn't balk at being seen by a psychiatrist because it was, after all, *special*."

In the early days of collaborative oncology group research, Jimmie would chide James and complain that cancer patients were asked every conceivable question about their physical functioning, but no one ever asked them "how do you feel emotionally?" Jimmie subsequently chaired the CALGB Quality of Life Committee for many years, pioneering the inclusion of psychological and emotional well being patient reported outcomes in quality of life measures and as a component of clinical outcomes in clinical trials.

At MSK, Dr. Holland conducted ground breaking clinical research examining the course and treatment of anxiety in cancer patients, examining the relationship of depression to pancreatic cancer and most significant demonstrating the utility of screening for distress in cancer patients.
As chair of the National Cancer Center Network Distress Management Guidelines since 1997, Jimmie's advocacy work led to the NCCN Distress Screening Guidelines being adopted in all NCI designated Cancer Centers. "Screening for Distress" became a practice that was a requirement for accreditation of cancer centers by the American College of Surgeons. Psycho-oncology programs became mandatory in all NCI-designated cancer centers.

In addition to her pioneering research at MSK, Dr. Holland established the largest Clinical and Research Training Post-doctoral Training Fellowship Programs for Psychiatrists and Psychologists in the world. The clinical programs and innovations created at MSK over the past 40 years helped establish Jimmie's department as the "Center of Excellence" in psycho-oncology worldwide.

Dr. Holland has received many awards recognizing her achievements over the course of her career. There are too many to list , however her awards include: The Medal of Honor for Clinical Research from the American Cancer Society, The Clinical Research Award from the American Association of Community Cancer Centers, The American Association for Cancer Research Joseph H. Burchenal Clinical Research Award, The Marie Curie Award from the Government of France, the Margaret L. Kripke Legend Award for contributions to the advancement of women in cancer medicine and cancer science from the MD Anderson Cancer Center, The T J Martell Foundation 2015 Women of Influence Award, and the Distinguished Alumnus Award from Baylor College of Medicine in 2016.

Dr. Holland stepped down as chairman of the MSK Department of Psychiatry and Behavioral Sciences in 2003, however she kept working full time, seeing patients, conducting research, training and supervising fellows, traveling the world lecturing and teaching, establishing a Geriatric Psycho-oncology Program in the department and committing her attention and energies to bring psycho-oncology to Africa through her work with the African Organization for Cancer Research & Training in Cancer (AORTIC).

Jimmie was seeing patients up until two days before her death. We've lost cancer pioneer, a remarkable woman, a once in a generation influencer. Her death is a profound loss for all of oncology.

The author is the Jimmie C. Holland Chair in Psychiatric Oncology and chairman of the Department of Psychiatry & Behavioral Sciences at Memorial Sloan Kettering Cancer Center.

AN APPRECIATION

Gerald Hanks, pioneering radiation oncologist, dies at 83

By Eric Horwitz

Gerald E. Hanks was a giant in the world of radiation oncology and oncology in general. It isn't often that we can say this and probably understate a person's significance and influence, but Jerry was one of those people. He died on Dec. 20, 2017, at the age of 83.

For those of us who were privileged to know him, work with him, learn from him and call him a friend, he will truly be missed. For many of us, caring for patients and hopefully curing their cancer is more than enough for our careers. But for Jerry, this was just the beginning.

Dr. Hanks was born in Ellensburg, Washington. He graduated from Washington State College with a basketball scholarship and received his medical degree from Washington University in St. Louis. For generations, radiation oncology was not a separate medical specialty. During radiology training, if you were interested in treating people's cancer with radiation, you became a therapeutic radiologist.

By the 1960s, the NCI recognized that this probably wasn't the best way to train physicians dedicated to oncologic care. Jerry Hanks, along with Zvi Fuks and Malcom Bagshaw, became one of the first three residents in the United States to be trained specifically as a radiation oncologist at Stanford University. After completing his residency, Jerry subsequently held academic faculty appointments at Stanford, the University of North Carolina, The University of California Davis, the University of Pennsylvania and Fox Chase Cancer Center in Philadelphia.

From 1971-1985, he practiced radiation oncology at the Radiation Oncology Center in Sacramento, Calif. where he provided leadership for a strong private practice radiation oncology program and successfully introduced clinical research into the community setting.

He returned to academic medicine in 1985 and served as chairman of the Department of Radiation Oncology at Fox Chase for 16 years until 2001, when he retired from medicine. He is credited with establishing the department's national prominence, and was honored by Fox Chase with the creation of the Gerald E. Hanks, MD, endowed chair in radiation oncology.

Dr. Hanks was the author of more than 300 scientific publications with a primary focus on prostate cancer. He held numerous important leadership positions in the American Society of Radiation Oncology, the American Radium Society, and the American College of Radiology and the Radiation Therapy Oncology Group. He was president of ASTRO and ARS. He was a member of the Board of Chancellors and chair of the Commission on Cancer and the Committee on Radiation Oncology Practice Accreditation of the ACR. During his service to ASTRO and the ACR, he played a critical role in preserving a single voice for radiation oncology and diagnostic radiology at a time of great change in health care practice. He received many honors including Gold Medals from ASTRO and the ACR.

I was talking about what an incredible person Jerry was with my family the other day, and my son asked me what was it that made Jerry so important in the field of radiation oncology. After thinking about it for a few minutes, I told him that Jerry basically developed and put into practice the way to safely deliver higher doses of radiation more precisely, thereby curing more cancers with fewer side effects.

This technique was called 3D conformal radiation therapy and it revolutionized the practice of radiation oncology in the 1980s and 1990s. It was first used to treat prostate cancer, but was subsequently used to treat many cancers including head & neck, lung, gastrointestinal and gynecologic malignancies. 3DCRT paved the way for even more precise techniques, including intensity modulated radiation therapy and stereotactic body radiation therapy, which we all routinely use today to treat people around the world with all different types of cancer.

At Fox Chase, his technology advancements included the first routine use of CT and MRI in planning radiation treatment in the United States and the use of ultrasound to improve the accuracy of each daily treatment.

And if that wasn't enough, he also pioneered the use of evidence-based outcomes to develop more effective ways to treat many different kinds of cancer with radiation, beginning in the 1970s as a leader of the Patterns of Care Studies and the Radiation Therapy Oncology Group.

The Patterns of Care studies were the first of their kind in an oncology specialty. They surveyed patterns of care in radiation oncology in the United States beginning in 1973, defined national standards for clinical care and reported outcome of treatment for various malignancies. These efforts prompted other specialties to undertake national quality assurance programs, with the assistance of technology developed by the Patterns of Care.

Dr. Hanks devoted his medical career to improving the outcome of men with prostate cancer. His legacy continues with the many residents and faculty he trained and mentored and whose careers he promoted as well as the many men who benefited from his innovative and visionary clinical research. These are just a few things that his colleagues sent me about Jerry after learning of his passing:

"Knowing this day would come doesn't lessen the impact. We have lost a true giant in the field, and one who caringly supported the development of his trainees and faculty. He set an example for us all. He will be sorely missed."

"He impacted all of our lives in a grand way. He was a special and selfless soul, gentle and kind, and will be missed by all who were fortunate to know him. He launched my career as a statistician in cancer research, and provided me with invaluable mentorship. I have never worked with, or known anyone else, quite like him."

"Jerry was my first boss and I am grateful for everything that he taught me… mostly about life."

I would be remiss if I didn't mention some of the other things important to Jerry, beginning with college basketball (especially the Washington State Cougars) and football. He could talk for hours with anyone about detailed strategy and standings and he loved to go to games. He tried to introduce some culture to our department with wine tastings (always on a Friday). He, himself, was a survivor of prostate cancer.

He is survived by his wife Dr. Barbara Fowble, four children (Dr. Stephen Hanks, Michael Hanks, Kimberly Hanks, and Leslie Hanks Angelacci), ten grandchildren and one great grandchild.

The author is the holder of the Gerald E. Hanks Chair of Radiation Oncology, and is a professor and chair of the Department of Radiation Oncology at Fox Chase Cancer Center.

IN BRIEF

Howard "Skip" Burris elected ASCO president for 2019-2020

Howard "Skip" Burris III was elected president of the American Society of Clinical Oncology for the term beginning in June 2019.

Burris is president of clinical operations and chief medical officer for Sarah Cannon, the cancer institute of HCA Healthcare. He is an associate of Tennessee Oncology, PLLC.

Burris completed his undergraduate education at the United States Military Academy at West Point, his medical degree at the University of South Alabama, and his internal medicine residency and oncology fellowship at Brooke Army Medical Center in San Antonio.

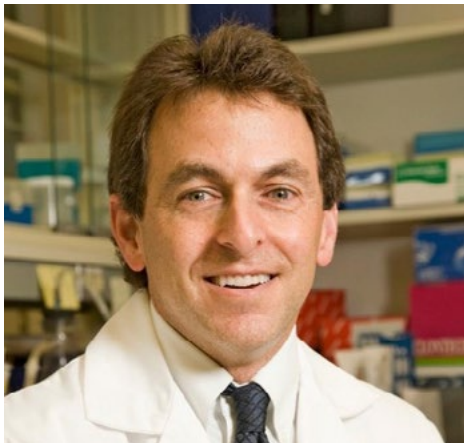
The following physicians will begin four-year terms as members of ASCO's Board of Directors starting in June 2018:

- **Laurie Gaspar**, treasurer. Gaspar is professor emeritus in the Department of Radiation Oncology at the University of Colorado.

- **Tracey Weisberg** was elected to a Community Oncologist seat. Weisberg is the lead physician of New England Cancer Specialists, and oversees medical house staff at the Maine Medical Center Oncology inpatient unit.

- **Tony Mok** was elected to an International Oncologist seat. Mok is the Li Shu Fan Medical Foundation Named Professor of Clinical Oncology and chair of clinical oncology at The Chinese University of Hong Kong. He co-founded the Lung Cancer Research Group.

- **A. William Blackstock** was elected to a Radiation Oncologist seat. Blackstock is professor and chair of the Department of Radiation Oncology at the Wake Forest University School of Medicine and director of the Clinical Research Program at the Comprehensive Cancer Center.



- **Lee Ellis** was elected to an Undesignated Specialty seat. Ellis is the William C. Liedtke Jr. Chair in Cancer Research and a professor in the Departments of Surgical Oncology and Molecular & Cellular Oncology at MD Anderson Cancer Center, as well as the vice chair of Translational Medicine at SWOG.

The following physicians will serve a three-year terms on the ASCO Nominating Committee:

- **N. Lynn Henry** will serve as the chair of the ASCO Nominating Committee in 2020-2021. Henry is an associate professor of internal medicine and interim division chief of oncology at the University of Utah and director of breast medical oncology at the Huntsman Cancer Institute.

- **W. Kimryn Rathmell** is the Cornelius A. Craig Professor of Medicine at Vanderbilt-Ingram Cancer Center and a professor of biochemistry at Vanderbilt University Medical Center. Rathmell is the vice president for the American Society of Clinical Investigation, chairing the Advocacy Committee and serving as board representative for the Federation of American Societies of Experimental Biology.

Hochster named associate director, clinical research, and chief of GI med/onc at Rutgers

Howard Hochster assumed the role of associate director for clinical research and chief of gastrointestinal medical oncology at Rutgers Cancer Institute, as well as director of cancer clinical research for oncology services at RWJBarnabas Health.

Hochster is an expert in the development of cancer clinical trials, gastrointestinal oncology and early phase cancer drugs.

Hochster, who is awaiting appointment as a distinguished professor of medicine in the Division of Medical Oncology at Rutgers Robert Wood Johnson Medical School, was most recently on the faculty at the Yale Cancer Center and the Yale School of Medicine, where he served as a professor of medicine, associate director for clinical sciences and the disease aligned research team leader for the Gastrointestinal Cancers Program. He also served as a clinical program leader for the Gastrointestinal Cancers Program at Smilow Cancer Hospital.

In his new roles, Hochster will oversee clinical research activities, which include therapeutic cancer clinical trials offered at Rutgers Cancer Institute and throughout the RWJBarnabas Health system.

Hochster, whose most recent clinical trials work focused on checkpoint inhibitors, is chair of the Gastrointestinal Cancer Committee of SWOG.

Prior to Yale, Hochster spent more than two decades at the former New York University Cancer Institute, where he led the Office of Clinical Trials and Developmental Therapeutics and held other leadership roles.

He is a medical director of the Chemotherapy Foundation and an associate editor of the Journal of the National Cancer Institute and an editorial board member of Gastrointestinal Oncology and Current Colorectal Cancer Reports.

Whitten named president of Taiho Oncology

Timothy Whitten was named president of Taiho Oncology Inc., a subsidiary of Taiho Pharmaceutical Co. Ltd.

Whitten, who until now has served as senior vice president and chief operating officer, will oversee corporate, commercial and clinical development-related functions at Taiho Oncology, as well as hold operational responsibility for Taiho Pharma Canada Inc. and Taiho Pharma Europe Ltd.

Whitten will continue to report to Taiho Oncology's departing president, Eric Benn, who will remain chief executive officer until his retirement on April 1, at which time Whitten also will be named CEO.

At that time, Whitten will report directly to Masayuki Kobayashi, president and representative director of Taiho, headquartered in Tokyo.

Whitten joined Taiho Oncology in 2013 as senior vice president and chief commercial officer to oversee the company's commercial functions and build Taiho Pharmaceutical's first commercial business unit in the West.

Whitten also was responsible for development and execution of the company's strategy for Lonsurf (trifluridine and tipiracil) tablets, Taiho Oncology's first approved product in the United States.

Whitten was promoted to senior vice president and chief operating officer in 2017, adding human resources to his responsibilities, as well as operations of Taiho Pharma Canada Inc.

Prior to joining Taiho Oncology Inc., Whitten served as president and CEO of Transave/Insmed from 2006 to 2012. During this time, he guided the company's lead product from the preclinical stage into a global phase III program. From 2001 to 2006, Whitten was employed by Pharmacyclics, where he served in roles, including senior vice president, marketing & sales, and business development.

Whitten spent 17 years at Bristol-Myers Squibb, where he served in various sales, marketing, and strategic planning roles. He also helped introduce Taxol into the U.S. oncology market.

Purdue Center for Cancer Research receives $10 million from Walther Cancer Foundation

Purdue University's Center for Cancer Research received a $10 million matching-funds gift from the Indianapolis-based Walther Cancer Foundation to advance its research in drug discovery, treatments and potential cures.

The gift is designed to inspire endowed gifts to Purdue's center to sustain it throughout its existence. It is the latest gift from the Walther Cancer Foundation, which has given more than $16 million in grants to Purdue over the years, including $4.2 million in the last three years before its latest gift.

The gift will be available for a variety of needs, such as faculty recruitment and retainment, needed equipment, and research in such areas as drug discovery and development; breast, pancreatic, prostate and other forms of cancer; and the role obesity plays in the disease.

METAvivor announces 2017 grant awards for metastatic cancer research

METAvivor Research and Support Inc., a non-profit organization dedicated to funding research for stage IV metastatic breast cancer, announced twelve grant awards totaling $1,650,000.

These research grants are focused on metastatic breast cancer. Since its founding in 2009, METAvivor has put 100% of donations into its peer-reviewed research grant program.

This is the eighth annual grant cycle funded by METAvivor, and this year, METAvivor is awarding grants from two award programs.

The newly established Young Investigator Award program is focused on funding grants for early career metastatic breast cancer researchers, while our standard awards program, now named the Translational Research Award, has changed to increase the amount of funding granted to $200,000 per grant for 2017.

METAvivor also announced the Kristin Keydel Endowment for Metastatic Breast Cancer Research Award and the Quinn-Davis Northwest Arkansas METSquerade Award. The grants named for donors and generous anonymous donors have helped METAvivor fund more exceptional research in 2017.

Following are the METAvivor 2017 grant recipients:

METAvivor Young Investigative Awards

- **Katherine Cook**, assistant professor, Wake Forest University: "Dietary considerations effecting lung metastatic therapeutic responsiveness and co-morbidities."
- **Joshua Donaldson**, fellow in oncology, Johns Hopkins University: "Resistance mechanisms to palbociclib in hormone positive metastatic breast cancer"
- **David Soto-Pantoja**, assistant professor, Wake Forest School of Medicine: "Anti-CD47 Immunotherapy as a treatment for metastatic breast cancer"

The Kristin Keydel Endowment for Metastatic Breast Cancer Research presents

- **Gina Sizemore**, postdoctoral fellow, Ohio State University: "Targeting novel tumor-stroma interactions in breast cancer brain metastases"
- **Rebecca Watters**, research assistant professor, University of Pittsburgh: "Discovery of Clinically Actionable Genes in Breast Cancer Bone Metastases"

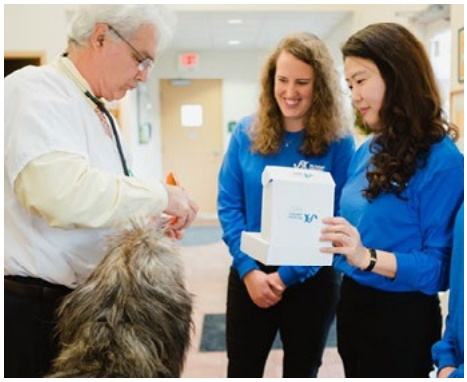
Research awards

- **Diana Cittelly**, assistant professor, University of Colorado: "Targeting BDNF/TrkB in brain metastases from young women with TNBC "
- **Michael Flister**, assistant professor, Medical College of Wisconsin: "Personalized therapy for curing metastatic breast cancer"
- **Melanie Hayden-Gephart,** assistant professor, Stanford University: "Halting the Progression of Breast Cancer Leptomeningeal Brain Metastases"

The Quinn-Davis Northwest Arkansas Metsquerade presents

- **Cheryl Jorcyk**, director of clinical/translational research, Boise State University: "High impact therapeutic for the elimination of breast cancer metastasis to bone"
- **James McIntyre**, research professor of radiology and radiological sciences, VUMC Nashville: "A Novel Self-Reporting Paclitaxel Prodrug without Systemic Neurotoxicity: Preclinical Assessment for Targeted Treatment of Metastatic Breast Cancer "
- **Vivek Mittal**, professor, Weill Cornell Medicine: "Targeting epigenetic regulator PRC2 as a therapy for established metastasis"
- **Partha Roy**, Professor of Bioengineering, Cell Biology, and Pathology, University of Pittsburgh: "Pharmacological inhibition of myocardin-family proteins as a novel strategy to combat metastatic breast cancer"

JAX starts canine cancer initiative to find predictors, treatments for humans, dog



The Jackson Laboratory launched the Tallwood Canine Cancer Research Initiative, which will create a biobank of dog tumors that the nonprofit biomedical research institution plans to use and share with researchers around the world to provide new insights into cures for cancer in humans and dogs.

JAX will identify and work closely with veterinary centers. When a canine patient at one of the JAX's veterinary partner organizations is diagnosed with a cancer of interest, its owner can opt to have the veterinarian donate their dog's tumor to TCCRI when it's removed during the dog's cancer treatment.

JAX will use the tumor to create a patient-derived xenograft cancer model and sequence each tumor model established, much like the organization's human PDX resource. PDX tumors are grown in mice, and can provide information including how cancer changes over time and what therapeutics are most effective. JAX will use these PDX models for its ongoing cancer research programs, as well as make them available to researchers around the world to accelerate the process of cancer treatment discovery.

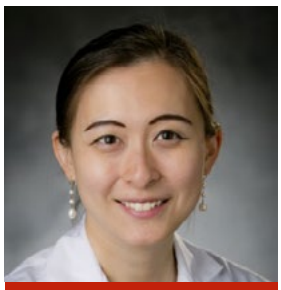
JAX investigators will also sequence the DNA from healthy canines of specific breeds.

JAX received a $500,000 gift for the Tallwood Canine Cancer Research Initiative from an anonymous Hartford-area donor. The TCCRI project began last month with the collection of DNA from the first healthy canine sample—the donor family's dog, Patrick, an Irish Wolfhound.

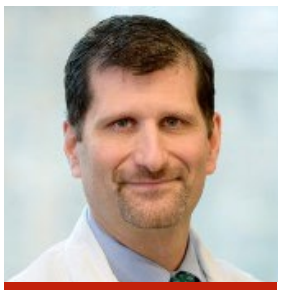
THE CLINICAL CANCER LETTER

TRIALS & TRIBULATIONS

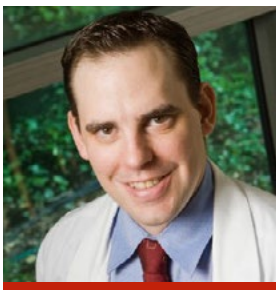
Cabozantinib in first-line treatment of metastatic renal cell carcinoma



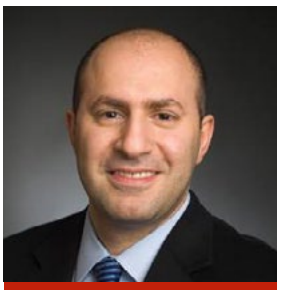
Tian Zhang
Duke Cancer Institute, Duke University, Durham, NC



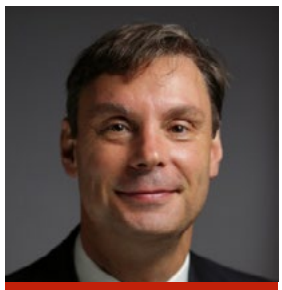
Michael J. Morris
Memorial Sloan-Kettering Cancer Center, New York, NY



Darren R. Feldman
Memorial Sloan-Kettering Cancer Center, New York, NY



Toni K. Choueiri
Dana Farber Cancer Institute, Harvard Medical School, Boston, MA



Daniel J. George
Duke Cancer Institute, Duke University, Durham, NC

Systemic therapies for metastatic renal cell carcinoma (mRCC) have expanded dramatically over the past 3 years.

Most recently, on Dec. 19, 2017 cabozantinib was approved by the FDA for use in untreated advanced renal cell carcinoma. This approval expands the label for cabozantinib, which was previously restricted to treatment for patients with prior anti-angiogenic treatment. The expansion to first-line therapy was based on an Alliance cooperative group trial termed CABOSUN, in which patients were randomized to either cabozantinib or sunitinib as initial treatment of mRCC.[1]

With the vascular endothelial growth factor (VEGF) pathway driving tumorigenesis and progression in clear cell RCC, first line treatment of mRCC has relied heavily on small molecule tyrosine kinase inhibitors (TKIs) of VEGF

receptors, including pazopanib or sunitinib. The COMPARZ study demonstrated non-inferiority between these two agents in this setting[2].

After pazopanib or sunitinib are employed in the first-line setting, resistance to VEGF targeted therapy presents a therapeutic challenge. In particular, tumors that express the receptors, MET and AXL, have been associated with poor prognosis and resistance to VEGF inhibitors[3].

Cabozantinib is a small molecule inhibitor with activity against both MET and AXL in addition to VEGF receptors. In RCC murine models, cabozantinib has been shown to rescue sunitinib resistance[4]. Therefore, cabozantinib could offer clinical benefit to patients previously treated with sunitinib. Support for this hypothesis was initially furnished by the METEOR trial[5], in which patients with advanced RCC who had previously received anti-angiogenic therapy clinically benefited from cabozantinib, leading to FDA approval on April 25, 2016.

To test whether MET and AXL are drivers of RCC disease progression on VEGF receptor targeted therapy required a different study. To test this hypothesis, we designed the CABOSUN study, which enrolled 157 patients with intermediate and poor risk (by International Metastatic Renal Cell Carcinoma Database Consortium [IMDC] criteria[6]), previously untreated mRCC and randomized them to either standard of care sunitinib or cabozantinib. 81% of patients were intermediate risk and 19% of patients had poor risk mRCC. The treatment arms were well-balanced.

A substantial number of patients in the study had bone metastases (37% of patients treated with cabozantinib and 36% of patients treated with sunitinib), and from prior analysis, patients who have bone metastases have worse outcomes than patients without bone metastases[7].

CABOSUN met its primary endpoint, demonstrating a superior investigator-assessed median progression-free survival (PFS) for cabozantinib compared to sunitinib (8.2 vs 5.6 months, respectively; HR 0.66, 95% CI 0.46-0.95, p=0.012)[1]. Compared to sunitinib, cabozantinib had similar grade 3/4 adverse events, including diarrhea (10%), fatigue (6%), hypertension (28%), palmar-plantar erythrodysesthesia (8%) and hematologic events (3%). The initial publication was based on a data cutoff of April 2016.

An independent review of the CABOSUN data applied additional FDA censoring rules: patients were censored if they started non-protocol cancer therapy or if they had more than 2 missing assessments. Similar to the initial results, the independent review confirmed the PFS benefit (median PFS 8.6 months with cabozantinib vs. 5.3 months with sunitinib, HR 0.48, 95% CI 0.31-0.74, p=0.0008)[8].

> When choosing between immunotherapy versus cabozantinib for treatment-naïve patients, we recommend considering the comorbidities of the patient as well as sites of metastases.

This benefit in PFS was shown across subsets of patients regardless of IMDC criteria or presence of bone metastases. The study did not show a statistically significant difference in overall survival (median 26.6 months vs. 21.2months, HR 0.80, 95% CI 0.53-1.21, p=0.29)[8] but was not powered for the overall survival (OS) endpoint.

Thus, cabozantinib is the first multi-targeted TKI to demonstrate superiority in delaying disease progression when compared to sunitinib in the first-line setting.

Over the past year alone, several treatments have improved first-line therapy for mRCC patients. In addition to cabozantinib, the phase III trial CheckMate 214, which randomized patients to the immunotherapy combination of ipilimumab and nivolumab versus sunitinib, also improved PFS as well as OS in treatment-naïve, intermediate and poor risk mRCC patients[9].

When choosing between immunotherapy versus cabozantinib for treatment-naïve patients, we recommend considering the comorbidities of the patient as well as sites of metastases. The immune mediated toxicities from combination immunotherapy should be carefully considered in patients who have underlying autoimmune disorders.

In addition, patients with metastases in sensitive sites such as the spinal column may need a faster response from cabozantinib instead of the slower time to response and possibility of tumor inflammation from immunotherapy.

Preliminary data also suggest that biomarkers could help with treatment decisions in the future. For example, MET expression may predict for benefit of cabozantinib[8], and there is a population of patients whose tumors express PD-

L1 who may have more favorable outcomes to nivolumab plus ipilimumab[9].

Is there a population of mRCC patients who could still derive benefit from sunitinib? In CheckMate-214, sunitinib demonstrated superior objective response rate (ORR) and PFS when compared to the ipilimumab-nivolumab combination in favorable risk mRCC patients[9].

Therefore, a select population of patients with RCC are still dependent on the VEGF pathway and can benefit from directed VEGF inhibition with sunitinib rather than immunotherapy. The activity of cabozantinib relative to sunitinib in the good-risk population has not been evaluated in prospective studies.

Outside of clinical trials, sunitinib also remains a preferred first-line treatment option for patients with non-clear cell RCC, given that studies of ipilimumab plus nivolumab as well as cabozantinib have been limited to patients with clear cell RCC, the predominant RCC histology.

Future research is needed to define the role of these agents in patients with non-clear cell subtypes of RCC. Trials currently enrolling patients with non-clear cell RCC include SAVOIR (NCT03091192) and PAPMET for papillary RCC (NCT02761057) as well as atezolizumab+bevacizumab (NCT02724878) and ipilimumab-nivolumab for non-clear cell RCC (NCT02982954).

In conclusion, the armamentarium of systemic agents available for first-line mRCC has expanded beyond pazopanib and sunitinib over the past year and now includes immunotherapy as well as cabozantinib. We await results from several ongoing phase III studies, in which VEGF and immunotherapy options are combined for mRCC patients.

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CLINICAL ROUNDUP

CAP publishes guideline to ensure accurate HPV testing in head and neck cancers

Certain head and neck cancers that are positive for high-risk types of human papillomavirus have a better prognosis and may need less aggressive treatment.

To help ensure that patients with these cancers are accurately diagnosed and effectively treated, the College of American Pathologists released its newest evidence-based practice guideline, "Human Papillomavirus Testing in Head and Neck Carcinomas," now available in Archives of Pathology and Laboratory Medicine.

An interdisciplinary, expert panel of pathologists, surgeons, radiation oncologists, medical oncologists, patients, and patient advocates developed the guideline, which recommends accurate assessments of a patient's high-risk HPV status, directly or by surrogate markers.

Based on a screening of 2,200 peer-reviewed articles and a review of evidence from 492 studies, the panel issued 14 final recommendations in the guideline. Notably:

- High-risk HPV testing should be performed on all patients with newly diagnosed oropharyngeal squamous cell carcinoma, including all histologic subtypes.
- HR-HPV testing should NOT be routinely performed on nonsquamous carcinomas of the oropharynx, nor on nonoropharyngeal primary carcinomas of the head and neck.
- Because marked overexpression of the tumor suppressor protein p16 is strongly associated with transcriptionally-active high-risk HPV, pathologists should perform HR-HPV testing by surrogate marker p16 immunohistochemistry on oropharyngeal tissue specimens. Additional HPV-specific testing may be done at the discretion of the pathologist, treating clinician, or in the context of a clinical trial.

For HPV-positive/p16 cases, tumor grade (or differentiation status) is not recommended. Resources to implement the new guideline are available on cap.org.

CAR-T therapy cancer study published in the New England Journal of Medicine

The study, "Axicagagene Ciloleucel (CD19 CAR T) in Refractory Large B-Cell Lymphoma," was led by Sattva Neelapu of the MD Anderson Cancer Center and Frederick Locke of the H. Lee Moffitt Cancer Center and Research Institute.

The CAR-T cell treatment used in the study, is offered by Kite Pharma. Two other companies, Novartis and Juno Therapeutics, are also developing CAR-T Cell therapies.

Based on results of the study, the FDA approved a CAR-T treatment called xicabtagene ciloleucel or Yescarta. The study included 111 patients from 22 centers, including John Theurer Cancer Center. The patients had refractory large B-cell lymphoma -who failed chemotherapy- or patients who relapsed early after stem cell transplantation.

The basis of this new cell therapy is to harness the patient's own T-cells, or white blood cells that are part of the immune system. T-cells are collected from the patient and sent to the manufacturing lab. There, the cells are genetically modified through introduction of a gene that instructs the cells to target and kill lymphoma cells. These genetically modified T-cells are then expanded in the lab before being infused back into the patient.

In the study, T-cells were successfully produced and expanded in 99 percent of patients. Eighty-four percent of patients responded, with 42 percent of all patients achieving a complete remission. More than half of all patients were alive as of 15.4 months.

Regarding toxicity, 95 percent of patients experienced at least one side effect that was severe. The most common adverse events of grade III or higher during treatment were neutropenia (in 78 percent of patients), anemia (in 43 percent), and thrombocytopenia (in 38 percent).

Grade III or higher cytokine release syndrome (released because of overstimulation of the immune system with CAR T-cells expanding) and neurologic events occurred in 13 percent and 28 percent of the patients, respectively. The use of low dose steroids and/or monoclonal antibody anti-IL6 receptor (to block one of the commonly found elevated cytokines IL6), tocili-

zumab, has dramatically helped manage toxicities.

Ongoing studies are looking at improving both toxicities and efficacy of CAR T-cell therapy using combinations particularly with checkpoint inhibitors.

Hackensack Meridian Health - John Theurer Cancer Center at Hackensack University Medical Center is the only New Jersey center that participated in a pivotal clinical trial of a groundbreaking cancer treatment, CAR-T cell therapy, which genetically modifies a patient's immune system to attack cancer cells.

André Goy, chairman and director, chief of lymphoma, and director of clinical and translational cancer research at John Theurer Cancer Center, is a co-author of the study, presented at the 59th Annual Meeting of the American Society of Hematology in the New England Journal of Medicine.

Cancer mortality in the U.S. continues decades-long drop

The cancer death rate dropped 1.7% from 2014 to 2015, continuing a decline that began in 1991 and has reached 26%, resulting in nearly 2.4 million fewer cancer deaths during that time.

The data is reported in Cancer Statistics 2018, the American Cancer Society's comprehensive annual report on cancer incidence, mortality, and survival. It is published in *CA: A Cancer Journal for Clinicians* and is accompanied by its consumer version: *Cancer Facts and Figures 2018*.

The report estimates that there will be 1,735,350 new cancer cases and 609,640 cancer deaths in the United States in 2018. The cancer death rate dropped 26% from its peak of 215.1 per 100,000 population in 1991 to 158.6 per 100,000 in 2015. A significant proportion of the drop is due to steady reductions in smoking and advances in early detection and treatment.

The overall decline is driven by decreasing death rates for the four major cancer sites: Lung (declined 45% from 1990 to 2015 among men and 19% from 2002 to 2015 among women); female breast (down 39% from 1989 to 2015), prostate (down 52% from 1993 to 2015), and colorectal (down 52% from 1970 to 2015).

Over the past decade, the overall cancer incidence rate was stable in women and declined by about 2% per year in men.

The report also finds that while the racial gap in cancer mortality continues to narrow, this mainly reflects progress in older age groups, and masks stark persistent inequalities for young and middle-aged black Americans.

Among all ages combined, the cancer death rate in 2015 was 14% higher in non-Hispanic blacks than in non-Hispanic whites, down from a peak of 33% in 1993. However, while the gap narrowed to 7% in those 65 or older, likely in part due to universal health care access for seniors through Medicare, mortality rates were 31% higher in blacks than in whites under 65, with much larger disparities in many states.

While the new report also finds that death rates were not statistically significantly different between whites and blacks in 13 states, a lack of racial disparity is not always indicative of progress. For example, cancer death rates in Kentucky and West Virginia were not statistically different by race, but are the highest of all states for whites.

Other highlights:

- The overall estimate of 1,735,350 cases for 2018 equals more than 4,700 new cancer diagnoses each day.
- Prostate, lung, and colorectal cancers account for 42% of all cases in men, with prostate cancer alone accounting for almost one in five new diagnoses.
- For women, the three most common cancers are breast, lung, and colorectal, which collectively represent one-half of all cases; breast cancer alone accounts for 30% all new cancer diagnoses in women.
- The most common causes of cancer death are lung, prostate, and colorectal cancers in men and lung, breast, and colorectal cancers in women. These four cancers account for 45% of all cancer deaths, with one in four cancer deaths from lung cancer.
- The lifetime probability of being diagnosed with cancer is slightly higher for men (39.7%) than for women (37.6%). Adult height has been estimated to account for one-third of the difference.
- Liver cancer incidence continues to increase rapidly in women, but appears to be plateauing in men. The long-term, rapid rise in melanoma incidence appears to be slowing, particularly among younger age groups. Incidence rates for thyroid cancer also may have begun to stabilize in recent years, particularly among whites, in the wake of changes in clinical practice guidelines.
- The decline in cancer mortality, which is larger in men (32% since 1990) than in women (23% since 1991), translates to approximately 2,378,600 fewer cancer deaths (1,639,100 in men and 739,500 in women) than what would have occurred if peak rates had persisted.

DRUGS & TARGETS

FDA approves Perjeta in adjuvant breast cancer

FDA has approved Genentech's Perjeta (pertuzumab), in combination with Herceptin (trastuzumab) and chemotherapy (the Perjeta-based regimen), for adjuvant treatment of HER2-positive early breast cancer at high risk of recurrence.

Genentech is a member of the Roche Group.

Patients should receive the adjuvant Perjeta-based regimen for one year (up to 18 cycles).

FDA has also converted the previously granted accelerated approval of the Perjeta-based regimen to full approval for neoadjuvant treatment of HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than two centimeters in diameter or node-positive). People receiving the neoadjuvant Perjeta-based regimen should continue Perjeta and Herceptin after surgery to complete one year of treatment.

The FDA-approved use of the Perjeta-based regimen for adjuvant treatment of HER2-positive EBC at high risk of recurrence is based on results of the phase III APHINITY study. At the time of the primary analysis with a median of 45.4 months follow-up:

- In the overall study population, Perjeta, Herceptin and chemotherapy significantly reduced the risk of invasive breast cancer recurrence or death by 18 percent compared to Herceptin and chemotherapy alone (HR=0.82, 95% CI 0.67-1.00, p=0.047).

- High-risk patients included patients such as those with lymph node-positive or hormone receptor-negative breast cancer. The subgroup results were as follows:

  - Lymph node-positive subgroup (HR=0.77, 95% CI 0.62-0.96)

  - Hormone receptor-negative subgroup (HR=0.76, 95% CI 0.56-1.04)

  - Hormone receptor-positive subgroup (HR=0.86, 95% CI 0.66-1.13)

  - Lymph node-negative subgroup (HR=1.13, 95% CI 0.68-1.86)

The most common severe (grade III-IV) side effects with the Perjeta-based regimen are low levels of white blood cells with or without a fever, diarrhea, decrease in certain types of white blood cells, decrease in red blood cells, fatigue, nausea and mouth blisters or sores. The most common side effects are diarrhea, nausea, hair loss, fatigue, nerve damage and vomiting.

The supplemental Biologics License Application for the Perjeta-based regimen for adjuvant treatment of HER2-positive EBC was granted Priority Review, a designation given to medicines the FDA has determined to have the potential to provide significant improvements in the treatment, prevention or diagnosis of a disease.

Perjeta is also approved for use in combination with Herceptin and docetaxel in people who have HER2-positive breast cancer that has spread to different parts of the body and who have not received anti-HER2 therapy or chemotherapy for metastatic breast cancer.

APHINITY (Adjuvant Pertuzumab and Herceptin IN Initial TherapY in Breast Cancer, NCT01358877/ BO25126/ BIG 4-11) is an international, phase III, randomized, double-blind, placebo-controlled, two-arm study evaluating the efficacy and safety of Perjeta plus Herceptin and chemotherapy compared to Herceptin and chemotherapy as adjuvant therapy in 4,805 people with operable HER2-positive EBC.

The primary efficacy endpoint of the APHINITY study is invasive disease-free survival, which in this study is defined as the time a patient lives without return of invasive breast cancer at any site or death from any cause after adjuvant treatment. Secondary endpoints include cardiac and overall safety, overall survival, disease-free survival and health-related quality of life. The study will continue to follow participants for ten years.

FDA approves Cabometyx for previously untreated advanced renal cell carcinoma

FDA approved Cabometyx (cabozantinib) tablets for the expanded indication of patients with advanced renal cell carcinoma.

FDA's priority review and approval of Cabometyx was based on results from the randomized phase II CABOSUN trial in patients with previously untreated RCC, which demonstrated a statistically significant and clinically meaningful improvement in progression-free sur-

vival versus sunitinib, a current standard of care.

The label expansion follows the initial FDA approval of Cabometyx in April 2016 for the treatment of patients with advanced RCC who have previously received anti-angiogenic therapy.

The expanded approval of Cabometyx is based on results of the phase II CABOSUN trial, which met its primary endpoint of improving PFS. According to the independent radiology review committee analysis of the data, Cabometyx, sponsored by Exelixis Inc., demonstrated a clinically meaningful and statistically significant 52 percent reduction in the rate of disease progression or death (HR 0.48, 95% CI 0.31-0.74, two-sided P=0.0008). Median PFS for Cabometyx was 8.6 months versus 5.3 months for sunitinib, corresponding to a 3.3 month (62 percent) improvement.

All causality grade III or IV adverse reactions occurred in 68 percent of patients receiving Cabometyx and 65 percent of patients receiving sunitinib.

The most frequent all causality Grade 3-4 adverse reactions (≥5 percent) in patients treated with Cabometyx were hypertension, diarrhea, hyponatremia, hypophosphatemia, palmar-plantar erythrodysesthesia, fatigue, increased ALT, decreased appetite, stomatitis, pain, hypotension, and syncope. Twenty-one percent of patients in the Cabometyx arm compared to 22 percent of patients receiving sunitinib discontinued treatment due to adverse events.

On May 23, 2016, Exelixis announced that CABOSUN met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in PFS compared with sunitinib in patients with advanced intermediate- or poor-risk RCC as determined by investigator assessment.

The CABOSUN study was conducted by The Alliance for Clinical Trials in Oncology and was sponsored by the National Cancer Institute-Cancer Therapy Evaluation Program under the Cooperative Research and Development Agreement withExelixis for the development of cabozantinib.

These results were first presented by Toni Choueiri at the European Society for Medical Oncology 2016 Congress, and published in the Journal of Clinical Oncology (Choueiri, JCO, 2016).

In June 2017, a blinded independent radiology review committee confirmed that cabozantinib provided a clinically meaningful and statistically significant improvement in the primary efficacy endpoint of investigator-assessed PFS. Results from the IRC review were presented by Dr. Toni Choueiri at the ESMO 2017 Congress.

CABOSUN was a randomized, open-label, active-controlled phase II trial that enrolled 157 patients with advanced RCC determined to be intermediate- or poor-risk by the IMDC criteria. Patients were randomized 1:1 to receive cabozantinib (60 mg once daily) or sunitinib (50 mg once daily, 4 weeks on followed by 2 weeks off).

The primary endpoint was PFS. Secondary endpoints included overall survival, objective response rate and safety. Eligible patients were required to have locally advanced or metastatic clear-cell RCC, ECOG performance status 0-2 and had to be intermediate or poor risk per the IMDC criteria (Heng, JCO, 2009). Prior systemic treatment for RCC was not permitted.

FDA approves Pfizer's Bosulif (bosutinib) for newly-diagnosed Ph+ CML

FDA approved a supplemental New Drug Application to expand the indication for Bosulif (bosutinib) to include adult patients with newly-diagnosed chronic phase Philadelphiachromosome-positive chronic myelogenous leukemia.

The sNDA was reviewed and approved under the FDA's Priority Review and accelerated approval programs based on molecular and cytogenetic response rates. Continued approval for this indication may be contingent upon verification and confirmation of clinical benefit in an ongoing long-term follow up trial.

Bosulif, sponsored by Pfizer, was first approved in September 2012 in the U.S. for the treatment of adult patients with chronic, accelerated or blast phase Ph+ CML with resistance or intolerance to prior therapy.

The approval was based on results from BFORE (Bosutinib trial in first line chronic myelogenous leukemia treatment), a randomized multicenter, multinational, open-label phase III study which showed Bosulif 400 mg was associated with a significantly higher rate of patients achieving major molecular response at 12 months (47.2%; 95% CI, 40.9-53.4) compared to the rate achieved in patients treated with imatinib 400 mg (36.9%; 95% CI, 30.8-43.0), a current standard of care (two-sided P=0.0200).

Complete cytogenic response rate by 12 months was 77.2% (95% CI: 72.0, 82.5) for patients treated with Bosulif compared to 66.4% (95% CI: 60.4, 72.4) for patients treated with imatinib (two-sided P=0.0075).

Pfizer and Avillion entered into an exclusive collaborative development agreement in 2014 to conduct the BFORE trial. Under the terms of the agreement, Avillion provided funding and conducted the trial to generate the clinical data used to support this application and other potential regulatory

filings for marketing authorization for Bosulif as first-line treatment for patients with chronic phase Ph+ CML. With this approval, Avillion is eligible to receive milestone payments from Pfizer. Pfizer retains all rights to commercialize Bosulif globally.

Bosulif (bosutinib) is an oral, once-daily, tyrosine kinase inhibitor, which inhibits the Bcr-Abl kinase that promotes CML; it is also an inhibitor of Src-family kinases.

In the U.S., Bosulif (bosutinib) is now indicated for the treatment of patients with newly-diagnosed chronic phase Philadelphiachromosome-positive chronic myelogenous leukemia and for the treatment of adult patients with chronic, accelerated or blast phase Ph+ CML with resistance or intolerance to prior therapy (first approved in September 2012).

A 400 mg tablet was also recently approved by the FDA in addition to the previously approved 100 mg and 500 mg strengths. The recommended dose for newly-diagnosed patients is 400 mg orally once daily with food. For patients who are resistant or intolerant to prior tyrosine kinase inhibitor therapy, the recommended dose is 500 mg orally once daily with food.

In Europe, Bosulif was granted conditional marketing authorization in March 2013 for the treatment of adult patients with Ph+ CML previously treated with one or more TKIs and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options. The European Medicines Agency (EMA) has also validated for review a Type II Variation application for use of Bosulif in the same patient population.

BFORE is a randomized, multicenter, open-label phase III study designed to assess the effectiveness and safety of Bosulif (bosutinib) as a first-line treatment for patients with chronic phase Ph+ CML.

The study enrolled 536 patients at multiple sites in North America, Asia and Europe. Patients were randomized 1:1 to receive Bosulif 400 mg or imatinib 400 mg, a standard of care, for the duration of the study.

The primary outcome was to show superiority of Bosulif over imatinib at 12 months by comparing MMR, or the proportion of patients in each arm whose levels of the Bcr-Abl1 kinase have dropped below 0.1%.

FDA approves Xgeva for prevention of skeletal-related events in multiple myeloma

Amgen said FDA has approved the supplemental Biologics License Application for Xgeva (denosumab) to expand the currently approved indication for the prevention of skeletal-related events in patients with bone metastases from solid tumors to include patients with multiple myeloma.

The approval is based on data from the pivotal phase III '482 study, which enrolled 1,718 patients.

"Up to 40 percent of patients remain untreated for the prevention of bone complications, and the percentage is highest among patients with renal impairment at the time of diagnosis," said Noopur Raje, director of the Center for Multiple Myeloma at Massachusetts General Hospital Cancer Center. "Denosumab, which is not cleared through the kidneys, offers multiple myeloma patients bone protection with a convenient subcutaneous administration, providing patients with a novel treatment option."

Xgeva is a fully human monoclonal antibody that binds to and neutralizes RANK ligand—a protein essential for the formation, function and survival of osteoclasts, which break down bone—thereby inhibiting osteoclast-mediated bone destruction.

The '482 study was an international, phase III, randomized, double-blind, multicenter trial of Xgeva compared with zoledronic acid for the prevention of skeletal-related events in adult patients with newly diagnosed multiple myeloma and bone disease.

In the study, a total of 1,718 patients (859 on each arm) were randomized to receive either subcutaneous Xgeva 120 mg and intravenous placebo every four weeks, or intravenous zoledronic acid 4 mg (adjusted for renal function) and subcutaneous placebo every four weeks.

The primary endpoint of the study was non-inferiority of Xgeva versus zoledronic acid with respect to time to first on-study skeletal-related event (pathologic fracture, radiation to bone, surgery to bone or spinal cord compression). Secondary endpoints included superiority of Xgeva versus zoledronic acid with respect to time to first on-study skeletal-related event and first-and-subsequent on-study skeletal-related event and evaluation of overall survival. Progression-free survival was an exploratory endpoint. The safety and tolerability of Xgeva were also compared with zoledronic acid.

The study met the primary endpoint, demonstrating non-inferiority of Xgeva to zoledronic acid in delaying the time to first on-study skeletal-related event in patients with multiple myeloma (HR=0.98, 95 percent CI: 0.85, 1.14; p=0.01). The secondary endpoints, delaying time to first skeletal-related event and delaying time to first-and-subsequent skeletal-related events, did not demonstrate superiority.

Overall survival was comparable between Xgeva and zoledronic acid, with a hazard ratio of 0.90 (95 percent CI: 0.70, 1.16; p=0.41). The median difference in progression-free survival favored Xgeva by 10.7 months (HR=0.82, 95 percent CI: 0.68-0.99; descriptive p=0.036). Median progression-free survival was 46.1 months (95 percent CI: 34.3 months, not estimable [NE], n=219) for Xgeva and 35.4 months (95 percent CI: 30.2 months, NE, n=260) for zoledronic acid.

Adverse events observed in patients treated with Xgeva were generally consistent with the known safety profile of Xgeva. The most common adverse reactions (greater than or equal to 10 percent) were diarrhea (34 percent), nausea (32 percent), anemia (22 percent), back pain (21 percent), thrombocytopenia (19 percent), peripheral edema (17 percent), hypocalcemia (16 percent), upper respiratory tract infection (15 percent), rash (14 percent) and headache (11 percent).

The most common adverse reaction resulting in discontinuation of Xgeva (greater than or equal to 1.0 percent) was osteonecrosis of the jaw. In the primary treatment phase of the '482 study, ONJ was confirmed in 4.1 percent of patients in the Xgeva group (median exposure of 16 months; range: 1 - 50) and 2.8 percent of patients in the zoledronic acid group (median 15 months, range: 1 - 45 months).

Kisqali receives breakthrough designation for HR+/ HER2- breast cancer

Kisqali (ribociclib) received FDA Breakthrough Therapy designation for initial endocrine-based treatment of pre- or perimenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative advanced or metastatic breast cancer in combination with tamoxifen or an aromatase inhibitor.

The drug is sponsored by Novartis.

The designation is based on positive results of the phase III MONALEESA-7 trial demonstrating Kisqali in combination with tamoxifen or an aromatase inhibitor as initial endocrine-based therapy significantly prolonged progression-free survival compared to endocrine therapy alone (median PFS 23.8 (95% CI: 19.2 months-not reached) vs. 13.0 months (95% CI: 11.0-16.4 months); HR=0.553; 95% CI: 0.441-0.694; p<0.0001).

A total of 672 women between ages 25 and 58 years were enrolled and randomized in the trial. All treatment combinations also included goserelin. Treatment benefit with Kisqali combination therapy was consistent compared to the overall population regardless of treatment with tamoxifen or aromatase inhibitor endocrine partners, and across predefined patient subgroups, the company said.

MONALEESA-7 was the first phase III trial entirely dedicated to evaluating a CDK4/6 inhibitor in premenopausal women with HR+/HER2- advanced breast cancer. The trial evaluated Kisqali in combination with oral endocrine therapies (tamoxifen or an aromatase inhibitor) and goserelin compared to oral endocrine therapy and goserelin in this patient population.

In subgroup analyses of median PFS by endocrine partner, Kisqali in combination with tamoxifen and goserelin demonstrated 22.1 months median PFS compared to 11.0 months for tamoxifen and goserelin alone; Kisqali in combination with an aromatase inhibitor and goserelin demonstrated 27.5 months median PFS compared to 13.8 months for an aromatase inhibitor and goserelin alone.

FDA accepts sBLA, grants priority review for Adcetris

FDA has accepted for filing a supplemental Biologics License Application for Adcetris (brentuximab vedotin) in combination with chemotherapy for the frontline treatment of patients with advanced classical Hodgkin lymphoma. The FDA granted Priority Review for the application, and the Prescription Drug User Fee Act target action date is May 1, 2018.

The submission of the supplemental BLA is based on positive results from a phase III clinical trial called ECHELON-1 that was designed to determine if Adcetris in combination with chemotherapy could extend modified progression-free survival in previously untreated advanced classical Hodgkin lymphoma patients.

Adcetris, sponsored by Seattle Genetics Inc., is an antibody-drug conjugate directed to CD30, a defining marker of classical Hodgkin lymphoma. Adcetris is being evaluated globally as the foundation of care for CD30-expressing lymphomas in more than 70 corporate- and investigator-sponsored clinical trials. Adcetris is currently not approved as a frontline therapy for Hodgkin lymphoma.

In October 2017, the FDA granted Adcetris Breakthrough Therapy Designation based on the ECHELON-1 study results. The FDA's Breakthrough Therapy Designation is intended to expedite the development and review of promising drug candidates for serious or life-threatening conditions. It is based upon clinical evidence of substantial improvement over existing therapies in one or more clinically significant endpoints.

The ECHELON-1 study evaluated a combination of Adcetris plus Adriamycin, vinblastine, dacarbazine compared to a recognized standard of care chemotherapy regimen, ABVD (which includes bleomycin), in frontline advanced classical Hodgkin lymphoma.

The positive results from the phase III ECHELON-1 trial were featured in the Plenary Scientific Session of the 59th American Society of Hematology Annual Meeting with simultaneous publication in the New England Journal of Medicine in December 2017. Results from the ECHELON-1 trial in 1,334 Hodgkin lymphoma patients included:

- The trial achieved its primary endpoint with the combination of Adcetris plus AVD resulting in a statistically significant improvement in modified PFS versus the control arm of ABVD as assessed by an Independent Review Facility (p-value=0.035). This corresponds to a 23 percent reduction in the risk of progression, death, or need for additional anticancer therapy. Per IRF assessment, the two-year modified PFS rate for patients in the Adcetris plus AVD arm was 82.1 percent compared to 77.2 percent in the control arm.

- The investigator assessment of modified PFS also demonstrated a statistically significant advantage for Adcetris plus AVD versus the control arm of ABVD (p-value <0.01).

- All secondary endpoints, including interim analysis of overall survival, trended in favor of the Adcetris plus AVD arm.

- The safety profile of Adcetris plus AVD in the ECHELON-1 trial was generally consistent with that known for the single-agent components of the regimen.

ECHELON-1 is a randomized, open-label, phase 3 trial is investigating ECHELON-1 plus AVD versus ABVD as frontline therapy in patients with advanced classical Hodgkin lymphoma.

The primary endpoint is modified PFS per Independent Review Facility assessment using the Revised Response Criteria for Malignant Lymphoma. Secondary endpoints include overall survival, complete remission and safety.

The multi-center trial was conducted in North America, Europe, South America, Australia, Asia and Africa. The study enrolled 1,334 patients who had a histologically-confirmed diagnosis of stage III or IV classical Hodgkin lymphoma and had not been previously treated with systemic chemotherapy or radiotherapy. The ECHELON-1 trial was conducted under a Special Protocol Assessment agreement from the FDA and the trial also received EMA scientific advice.

ECHELON-1 is being evaluated broadly in more than 70 clinical trials, including three phase III studies: the completed ECHELON-1 trial in frontline classical Hodgkin lymphoma, the ongoing ECHELON-2 trial in frontline mature T-cell lymphomas, and the ongoing CHECKMATE 812 trial of ADCETRIS in combination with Opdivo (nivolumab) for relapsed/refractory Hodgkin lymphoma.

FDA grants breakthrough designation for Avelumab in combination with Inlyta in RCC

FDA has granted Breakthrough Therapy Designation for Avelumab in combination with Inlyta (axitinib) for treatment-naïve patients with advanced renal cell carcinoma.

This is the second Breakthrough Therapy Designation granted to Avelumab, sponsored by Merck KGaA and Pfizer Inc.

The Breakthrough Therapy Designation is based on the preliminary evaluation of clinical data from JAVELIN Renal 100, a global phase Ib study assessing the safety and efficacy of avelumab in combination with Inlyta for the treatment of treatment-naïve patients with advanced RCC.

Updated results from this phase Ib study were presented at the 2017 American Society of Clinical Oncology Annual Meeting. The FDA previously granted avelumab Breakthrough Therapy Designation for the treatment of patients with metastatic Merkel cell carcinoma whose disease has progressed after at least one previous chemotherapy regimen.

The clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs and over 7,000 patients evaluated across more than 15 different tumor types.

This includes JAVELIN Renal 101, a randomized, phase III, open-label, multicenter trial investigating avelumab in combination with Inlyta versus sunitinib as a first-line treatment option for advanced RCC, which recently completed recruitment.

In addition to RCC, cancer studies in the JAVELIN program include non-small cell lung cancer, breast cancer, head and neck cancer, Hodgkin's lymphoma, melanoma, mesothelioma, MCC, ovarian cancer, gastric/gastroesophageal junction cancer, and urothelial carcinoma.

FDA grants orphan drug designation to Aptose Biosciences for CG'806 in AML

FDA has granted orphan drug designation to CG'806, a highly potent pan-FLT3/pan-BTK inhibitor, for the treatment of patients with acute myeloid leukemia.

AML cells utilize multiple forms of the FLT3 receptor tyrosine kinase and other pathways to promote rapid proliferation and to escape the inhibitory activities of many therapeutics. CG'806 is a highly potent inhibitor that simultaneously targets all known forms of FLT3 and other key oncogenic pathways that drive the proliferation of AML cancer cells, thereby providing CG'806 with a broad range of activity against AML and a strategy to delay mutational escape.

CG'806, sponsored by Aptose Biosciences Inc., is an oral, first-in-class pan-FLT3/pan-BTK inhibitor. This small molecule demonstrates potent inhibition of all wild type and mutant forms of FLT3 tested (including internal tandem duplication and mutations of the receptor tyrosine kinase domain and gatekeeper region), suppresses multiple oncogenic pathways operative in AML, eliminates AML tumors in the absence of toxicity in murine xenograft models, and represents a potential best-in-class therapeutic for patients with FLT3-driven AML.

Likewise, CG'806 demonstrates potent, non-covalent inhibition of the wild type and Cys481Ser mutant forms of the BTK enzyme, as well as other oncogenic kinases operative in B cell malignancies, suggesting CG'806 may also be developed for CLL and MCL patients that are resistant/refractory/intolerant to covalent BTK inhibitors.

FDA accepts regulatory submission for Tagrisso in 1st-line EGFR-mutated NSCLC

AstraZeneca said the FDA has accepted a supplemental New Drug Application for the use of Tagrisso (osimertinib), a third-generation, irreversible epidermal growth factor receptor tyrosine kinase inhibitor with clinical activity against central nervous system metastases, in the 1st-line treatment of patients with metastatic non-small cell lung cancer whose tumors have EGFR mutations (exon 19 deletions or exon 21 (L858R) substitution mutations).

The FDA has granted Tagrisso Priority Review status, and previously granted Breakthrough Therapy Designation for TAGRISSO in the 1st-line treatment of patients with metastatic EGFR mutation-positive NSCLC.

The submission acceptance is based on data from the phase III FLAURA trial, in which Tagrisso significantly improved progression-free survival (PFS) compared to current 1st-line EGFR-TKIs, erlotinib or gefitinib, in previously-untreated patients with locally advanced or metastatic EGFRm NSCLC.

On Sept. 28, 2017, the NCCN Clinical Practice Guidelines in Oncology were updated to include the use of Tagrisso in the 1st-line treatment of patients with locally advanced or metastatic EGFRm NSCLC. The use of Tagrisso in this indication is not yet approved by FDA.

Tagrisso once-daily tablets are approved by the FDA for the treatment of patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after an EGFR TKI therapy.

FDA grants priority review for Apalutamide in non-metastatic castration-resistant prostate cancer

Janssen Biotech Inc. said FDA has granted priority review designation for the New Drug Application for apalutamide, an investigational, next-generation oral androgen receptor inhibitor for the treatment of men with non-metastatic castration-resistant prostate cancer. Currently, there are no FDA-approved treatments for patients with non-metastatic CRPC.

The Priority Review designation means FDA's goal is to take action on an application within six months of receipt, compared to 10 months for Standard Review. The FDA has assigned a Prescription Drug User Fee Act target date of April 2018 to render a decision on the apalutamide application.

The NDA submission for apalutamide, which was completed on Oct. 10, 2017, was based on phase III data from the pivotal ARN-509-003 (SPARTAN) clinical trial, which assessed the safety and efficacy of apalutamide versus placebo in men with non-metastatic CRPC who have a rapidly rising prostate specific antigen despite receiving continuous androgen deprivation therapy.

The primary endpoint of this study was metastasis-free survival. MFS is the time from randomization to first evidence of confirmed metastasis, or time to death. The SPARTAN study results have been accepted for oral presentation at the ASCO Genitourinary Cancers Symposium Feb. 8, 2018, in San Francisco.

Apalutamide is an investigational, next-generation oral androgn recep-

tor inhibitor that inhibits the action of androgen in prostate cancer cells, and prevents binding of androgen to the androgen receptor, and translocation of the androgen receptor to the nucleus of the cancer cell.

Janssen and Legend Biotech enter deal to develop CAR-T therapy

Janssen Biotech Inc., a Janssen Pharmaceutical Company of Johnson & Johnson, said that it has entered into a worldwide collaboration and license agreement with Legend Biotech USA Inc. and Legend Biotech Ireland Limited, subsidiaries of Genscript Biotech Corp., to develop, manufacture and commercialize a chimeric antigen receptor T-cell drug candidate, LCAR-B38M, which specifically targets the B-cell maturation antigen. LCAR-B38M is currently accepted for review by the China Food and Drug Administration and in the planning phase of clinical studies in the United States for multiple myeloma.

LCAR-B38M is the first CAR-T therapy accepted for review by the CFDA. Under the agreement, Legend will grant Janssen a worldwide license to jointly develop and commercialize LCAR-B38M in multiple myeloma with the Legend team of experts. Janssen will record worldwide net trade sales, except for sales made in Greater China.

The companies have entered into a 50/50 percent cost-sharing/profit-split arrangement, except in Greater China, where Janssen and Legend have a 30/70 percent cost-sharing/profit-split arrangement. Janssen will make an upfront payment of $350 million and additional payments based upon the achievement of development, regulatory and sales milestones.