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THE CANCER LETTER

Inside information on cancer
research and drug development

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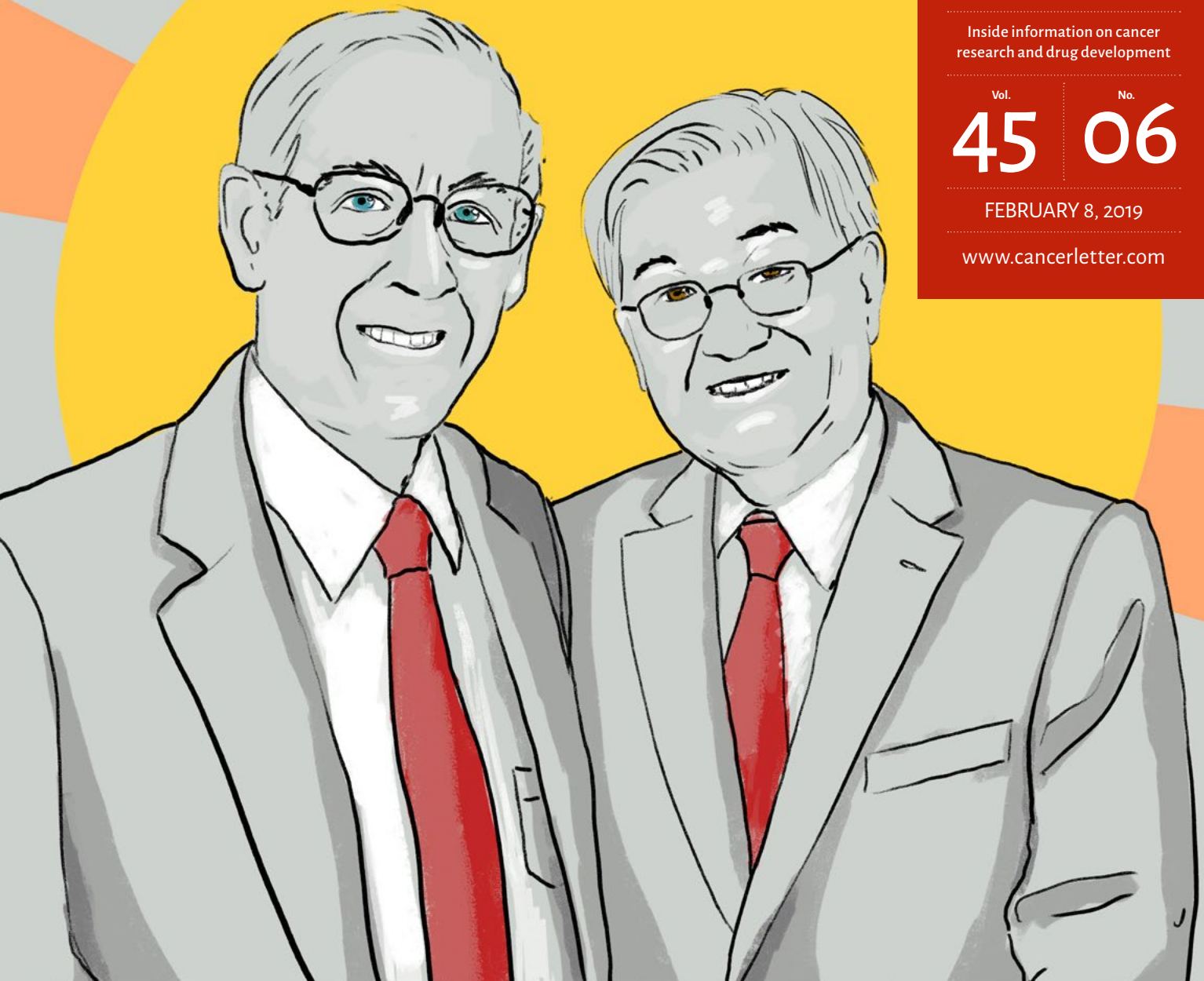
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TWO SINGULAR MEN SHARED AN UNCOMMON GREATNESS: WAUN KI HONG AND JOHN MENDELSOHN

Waun Ki Hong and John Mendelsohn were singular forces who combined to change the world of oncology and, in the process, the lives of countless trainees, faculty, patients, and families.

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GUEST EDITORIAL

TWO SINGULAR MEN SHARED AN UNCOMMON GREATNESS: WAUN KI HONG AND JOHN MENDELSON

Waun Ki Hong and John Mendelsohn were singular forces who combined to change the world of oncology and, in the process, the lives of countless trainees, faculty, patients, and families.



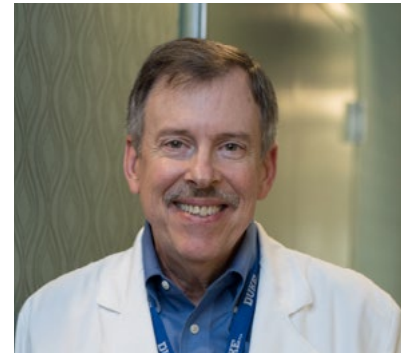
Scott M. Lippman

Director, Moores Cancer Center, associate vice chancellor, and Chugai Pharmaceutical Chair, UC San Diego; adjunct professor and former chief of the Section of Head and Neck Medical Oncology and Charles A. LeMaistre Distinguished Chair, Department of Thoracic/Head and Neck Medical Oncology, MD Anderson Cancer Center



Daniel D. Karp

Professor, Department of Investigational Cancer Therapeutics, formerly in the Department of Thoracic/Head and Neck Medical Oncology, MD Anderson; and former faculty, Boston Veterans Administration Medical Center under Dr. Hong, transitioning to his leadership position at the Boston VA when Ki left in 1984 to go to Houston



James L. Abbruzzese

Duke Cancer Institute Distinguished Professor of Medical Oncology; chief, Division of Medical Oncology; associate director for clinical research; and former chair of GI Medical Oncology and the Waun Ki Hong Distinguished Professor of Translational Medicine, MD Anderson

After these giants of cancer research and treatment died last month—they died five days apart—much was said about their careers and awards, of which there were many. All of this was important, but it's done, and now we can look at some of the timeless and instinctive leadership ingredients that shaped Ki's and John's success.

Through the course of many interactions, their approach to life synergized with each other, and they genuinely became the legends that they created. The relationship was not superficial. They were equals, and they took the time to learn from each other. They worked and played (tennis) together, they discussed programs and science, and in the end, they took care of each other. Whether they explicitly discussed leadership principles we may never know, but the closeness of the relationship suggests that they communicated deeply about how to work effectively in the context of complex academic and scientific systems to accomplish their personal goals while promoting institutional objectives and the work and careers of others.

Those of us lucky enough to have been mentees and colleagues of Ki and John experienced the unique dynamism and influence of each. *What* they did, and their impact, is a matter of public record; *how* they did it is another matter altogether.

Over the past month, we have deeply reflected on our history and experiences with Ki and John, and found ourselves researching little-known facets of their careers, gaining insights by tracking down students and colleagues who were delighted to reminisce and recall deeply etched, fond memories of these men, reaching as far back as the early 1970s.

We were struck by how Ki's and John's approaches, attitudes and outlook, decisions and dispositions made them the leaders they were. Though much

is written on the science of leadership, Ki and John, through their individual and joint accomplishments, could have written a fine book on the applied art of leadership, a few of the themes of which are presented below.

While technology and scientific methodology dramatically changed over Ki's and John's careers, the leadership ingredients have stood the test of time...

You never know when a routine or chance meeting could become a career-defining moment.

Both men made the most of even seemingly small opportunities when they presented themselves; and created their own breaks—such as when a Harvard undergraduate (John) knocked on the door of a new assistant professor named James Watson. Recognize that each encounter can leave an enduring impression. Cultivate “presence,” and preparation, to make small interactions noteworthy.

For Ki, it was a 1973 fellowship interview at Sloan Kettering, during which Irwin Krakoff, then chief of the Medical Oncology Service, could discern through the difficult English the intense passion, insight and focus that characterized Ki's early career. Intrigued, Krakoff kept an eye on Ki during his fellowship and beginning of his faculty career at Boston Veterans Affairs; taking note of Ki's incredible track-record of bringing precision and incisiveness to challenging clinical trials.

Krakoff was also impressed by Ki's capacity to work (he often said, “I only consider myself of average intelligence, but I can out-work most people”); absorbing everything he could learn during fellowship from the likes of Joseph Burchenal, David Karnofsky, and Robert Wittes, as he embraced very difficult clinical problems. Ki's

early faculty career at the Boston VA, focused on head and neck cancer, developing a series of interrelated and innovative clinical trials designed to interrupt this disease process, ranging from neoadjuvant chemotherapy to chemoprevention, each at the cutting edge of translational research.

Krakoff was recruited to MD Anderson in 1983 to elevate the academic stature of the Division of Medicine; a year later (and 10 years after a memorable fellowship interview), Ki was recruited to bring rigor to the clinical trials program as chief of the Section of Head and Neck Medical Oncology, then Charles A. LeMaistre Distinguished Chair of the Department of Thoracic/Head and Neck Medical Oncology at MD Anderson. On a related note, lasting impressions during his fellowship led Wittes, who had moved to the NCI Cancer Therapy Evaluation Program, to connect him several years later with surgeon Greg Wolf, who led the NCI Head and Neck Contracts Program HNCP-178, which set the stage for the pair to design and lead the landmark VACSP-268 laryngeal cancer preservation trial.



What they did, and their impact, is a matter of public record; how they did it is another matter altogether.



For John, it was during his residency at the Brigham and Women's Hospital. A chance meeting with a visiting professor from NIH, Eugene Braunwald,

would turn out to be a defining moment of his career.

Braunwald recognized early on that John had inherent leadership “gifts”: drive, vision, charisma. Several years later, while completing a hematology-oncology fellowship at Washington University, John received a call from Braunwald, who had moved to the University of California San Diego (UCSD) in 1968 as the founding chair of the Department of Medicine, where he wanted to build a strong presence in oncology.

He thought of John, introduced him to hematology division chief Mickey Goulian, who immediately recognized John’s talents and capabilities. They recruited John to UCSD in 1970, enticing him to break from his established Ivy League roots with the opportunity to literally “build oncology from the ground up” at this exciting, vibrant 2-year-old university.

Foster relationships with colleagues and competitors to build mutual respect and advance the field.

Ki and John were masters at convincing and motivating people to join them and collaborate, using many strategies known to build relationships. John shaped and transformed three major cancer centers while launching and driving the era of targeted therapy.

Yet, we highlight Ki’s approach to this principle because of its uniqueness as a tactic in academic medicine. Though we doubt Ki ever read a leadership book, he clearly understood the techniques embodied in the genius of Abraham Lincoln, as outlined in the *Team of Rivals* by Doris Kearns Goodwin.

Ki had the innate ability to cultivate relationships with colleagues and competitors by simultaneously competing with and promoting the interests of these individuals. With deep political



Though much is written on the science of leadership, Ki and John, through their individual and joint accomplishments, could have written a fine book on the applied art of leadership.



intuition, Ki built a team of trusted friends, colleagues and even rivals to advance cancer research and care.

He found a way to allow each of his competitors—including detractors—to contribute to cancer medicine, where they could achieve personal success, thereby advancing the field and, intended or not, simultaneously enhancing Ki’s stature. Throughout his career, Ki devoted considerable time and effort to elevating the careers of others—nominating and passionately advocating colleagues and competitors alike for major awards and accolades.

This tactic was simultaneously a selfless act, yet also one with great returns on investment, generating longstanding mutual respect and admiration. The success of this strategy was iterated throughout his career, and with each success became a self-reinforcing

aspect of Ki’s highly effective interactions with others. This was a political genius on par with that of Lincoln.

Think broadly, look ahead, recognize and promote talent.

John was recruited to UCSD to build an oncology program, but his expertise was as a hematology physician-scientist with additional fellowship training at the NIH, leading a large basic lab effort.

He knew he needed to bring a national leader in solid tumor clinical trials, so in 1976, the year John became the founding UCSD Cancer Center Director, he recruited the late Mark Green, one of the most highly respected oncologists in the United States, famous for his encyclopedic knowledge of clinical oncology (and memorizing medical record numbers of his patients).

John was always looking for ways to expand the breadth and depth of the UCSD Cancer Center within his modest budget. He successfully promoted and leveraged academic and academic-industry partnerships, and passionately engaged community leaders.

His broad vision is illustrated by his early years at UCSD, building the cancer program and center to encompass very basic studies of T-cell receptor biology, advancing disruptive monoclonal technology and establishing a nascent effort in community engagement.

In 1981, John recruited Georgia Sadler to be the associate director for administration, also realizing that her doctoral training in public health would be a real asset in helping him to expand the breadth of the center.

He supported her efforts to create public education and awareness programs highlighting the importance



Scott M. Lippman, MD

Director, Moores Cancer Center
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**VIDEO TRIBUTE CELEBRATING THE LEGACY OF WAUN KI HONG, MD,
JAN. 24, 2019, MD ANDERSON CANCER CENTER.**

of cancer prevention and clinical trial participation. This outreach effort had a strong regional focus on reducing cancer disparities, placing meaningful value on what we now call “catchment area,” making John one of the nation’s first directors of an NCI-designated cancer center to use community-campus partnerships as an effective cancer control strategy.

Embrace difficult challenges that address simple, compelling, and worthy questions.

Ki and John developed groundbreaking, yet straightforward, simple and compelling research hypotheses that addressed meaningful problems.

While simple in retrospect, each breakthrough was incredibly difficult and challenging to operationalize and implement, requiring tenacity, resilience and creativity in the face of opposition and scientific concerns regarding the validity of their research ideas and feasibility.

For example, though the idea behind Ki’s Biomarker-Integrated Approaches

of Targeted Therapy for Lung Cancer Elimination (BATTLE) study was simple and compelling—base targeted drug selection on *current* tumor biology—it was unprecedented and prompted vigorous debate, skepticism, and even ethical resistance.

The controversy centered on the risk of the core needle re-biopsy required to base drug selection on current biology in the second line setting, versus the risk of inaccurately selecting drug therapy or pathway targets from archival diagnostic tissue.

Despite the skepticism, BATTLE established the feasibility of a challenging precision therapy protocol design that has become an established approach in cancer medicine.

Related to his principle of simple, straightforward hypotheses, Ki designed trials to answer important questions, contributing valuable information, regardless of the result—this was his “no lose approach” to cancer research.

In 1980, John’s groundbreaking hypothesis that launched the era of targeted therapy was, at its core, quite sim-

ple—make an antibody to prevent the growth factor-receptor connection, in this case epidermal growth factor receptor (EGFR) to block cell proliferation.

The hypothesis, however, was based on circumstantial evidence, including basic studies of transferrin- and acetylcholine-receptor biology, but no direct experimental data. In fact, prevailing data revealed that monoclonal antibodies functioned as agonists in this setting. Unprecedented, uncertain, and unfunded, John partnered with Gordon Sato, to push the idea to reality through initially scraping together funds for preliminary hybridoma studies, screening thousands of antibodies over several years to find a lead compound (225) with strong antagonist, blocking activity. John moved to Sloan Kettering in 1985, continuing his 225 work, and led seminal studies driving the development of 4D5 and Herceptin with Rakesh Kumar and José Baselga.

These are but a few examples of the approach to leadership embodied and employed by these two great men. There were many similarly important principles in other aspects of their careers, including seamlessly integrating education and training into the fabric of cancer research and care: creatively designed and funded innovative and transformational training mechanisms such as an advanced scholars program.

Having the incredible fortune to work with them over many years, as well as listening to the stories told by former students and colleagues, was exciting and compelling. Ki and John didn’t write an actual book about their leadership experiences, but they “wrote the book,” figuratively, and that bears noting—and retelling.

Read more: For a more in-depth look at the lives of these two extraordinary and inspirational individuals, please read our [tribute in Cancer Cell](#), publishing on Feb. 11, 2019. (The link will go live on the day of publication.)

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

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CONVERSATION WITH
THE CANCER LETTER

NYU receives NCI Comprehensive Cancer Center designation

“

I promised the Perlmutter and the dean that we would get comprehensive status in five years, but my friend Kwok Wong, in a different context in a meeting said, ‘You should go big or go home.’

”



Benjamin G. Neel

Director,

Laura and Isaac Perlmutter Cancer Center, NYU Langone Health

The Laura and Isaac Perlmutter Cancer Center at NYU Langone Health received the Comprehensive Cancer Center designation from NCI.

The announcement was made Feb. 6. Now, NCI has 50 comprehensive cancer centers across the U.S., three of them in New York City. The city also has two clinical cancer centers.

When Benjamin G. Neel accepted the job of director of the cancer center in 2014, he promised to attain the comprehensive designation after two five-year cycles. Since he took the job at mid-cycle, this would have been 2023.

“It’s five years ahead of when we planned to do it. I promised the Perlmutter and the dean [Robert I. Grossman, dean and CEO of NYU Langone] that we would get comprehensive status in five years, but my friend Kwok Wong, in a different context in a meeting said, ‘You should go big or go home,’” Neel said to *The Cancer Letter*.

To meet this challenge—or for that matter just to stay afloat—Neel had to recruit an entire level of leadership, and do it rapidly.

“When I came here, there was an unprecedented number of vacancies in the leadership positions,” Neel said. “That was both a challenge and a tremendous opportunity, because you don’t usually get this kind of situation. We had the kind of leadership vacancies that you usually would see in a place that was starting out and was trying to grow into a designated cancer center.

“We were, actually, lucky that we were able to fill so many of these positions and get a lot of improvement early. And so, I felt that it was worth taking a shot at comprehensive. I felt we’d give it our best shot, and by the time we actually put the grant together and read it

and everything, I felt that we deserved comprehensive status for the grant. But I think up until then, it was a 50/50 chance. And I also felt that regardless of what the site visit team said, we were a comprehensive cancer center.”

NYU was among the first cancer centers to receive NCI-designation and comprehensive status, but lost it in the 1990s, regaining the clinical cancer center designation in 2003.

Since NYU received an overall “outstanding” rating, it will receive a little over \$2.35 million in new funding each year (direct costs) for its research programs, shared resources, educational and community outreach activities.

This adds up to nearly \$20 million for the five-year grant. This represents a 51 percent increase from our last grant, one of the largest increases to any cancer center, NYU officials said.

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

Paul Goldberg: First, congratulations on the designation.

Benjamin Neel: Thank you. It was a long haul, but, you know, everybody’s pretty happy, so it makes it worthwhile.

There’s an often-made, often-quoted observation that once you’ve seen one cancer center, you’ve seen one cancer center.

BN: That’s probably true. It’s a good observation.

Well, what is your center like, how is it different from all the others?

BN: I think what’s really the big story here is that when I came here, we had a unique opportunity in that we were an NCI-designated cancer center, and we’re embedded in a major medical center.

But, on the other hand, when I came here, there was an unprecedented number of vacancies in the leadership positions, pretty much unprecedented for a designated cancer center.

That was both a challenge and a tremendous opportunity, because you don’t usually get this kind of situation. We had the kind of leadership vacancies that you usually would see in a place that was starting out and was trying to grow into a designated cancer center.

And that, plus the \$50 million gift from the Perlmutter, gave us the opportunity to rapidly reshape the cancer center almost from the ground up. We were in some ways a new cancer center, and, also, we were coming from the standpoint where we’re already designated and embedded in a very rich medical school that had a lot of strengths in the discovery or basic science areas.

It’s literally no exaggeration that the entire leadership team was changed in the three years before the grant. New deputy director, a new associate director, new associate directors, of basic translational, population sciences—basically every single leadership position.

And I would say, I don’t remember if it’s half or a little bit more than half of the program co-directors. We’re basically a new cancer center, and at the same

time, we're starting from the standpoint of a designated cancer center.

That's the big story here, and it's in the context of similar changes that were going on in advance of that for about five years at the medical school, where the medical school has gone from a solid middle-tier medical school to a medical school that's ranked third in the country.

I think the story that makes us different than others is that we're a turnaround story, or a transformation story, an entirely new cancer center from where we were four years ago.

And I think that that was an unusual combination of circumstances that allowed that to happen.

How did you do it?

BN: How did I do it? It's hard to summarize.

First of all, I'm very fortunate in the sense that I had spent eight years in Toronto, at Princess Margaret Cancer Centre, so I had actually seen firsthand what a really strong clinical research operation looked like. In Toronto, we had world-class clinical trials in phase I and phase II in the drug development program.

And, at the same time, we had a strong basic science environment. So I had some ideas in advance about what needed to be done here at NYU.

When I came to Toronto, my clinical colleagues there were very skeptical about having a basic scientist come in as the research director, because I think that there was sort of a tension between the clinical side and the research side there.

And I rapidly realized that the operation actually starts from the clinical side, and then the clinical engine or the clinical operation helps support the basic science, not the other way around.

And I think that many of my basic science colleagues haven't benefited from that insight when they take a job like this, or maybe they don't know much about the clinical side.

When I came here, I looked at the landscape. We spent about six months having a relatively truncated strategic planning process. When I was in Toronto, we took a year to do that, because we had more time.

But here, with the impending cancer center grant, and also with the need to really fill the leadership positions, there was just an incredible assortment of problems. The clinical trial operation was really embryonic and dysfunctional. We were short-handed in multiple areas. We didn't have these leadership positions filled. We had to make these decisions reasonably quickly.

And my general feeling is that cancer centers should have full service teams in major disease areas, where you have basic science translation to the clinic and then back, and population research, too.

When I came here, melanoma was the only area that was even close to being a full service or a fully integrated program, where you go bench to bedside and back, and even that wasn't that strong. And then we had these leadership vacancies.

I think it's important to figure out what your exact priorities are, and my priorities were twofold.

One was to fill those leadership positions, and the other one was to build three to five full-service bench-to-bedside-to-bench clinical research translational teams.

I'm a big football fan, so this has been a very good week for me, because I'm a Patriots fan.

It's been a good week all along: Patriots win the Super Bowl, \$75 million gift [to PCC], and then the comprehensive cancer center designation, all in four days.

That's pretty good.

I know from football, in the 70s and 80s, when I was growing up, that there were two major strategies for football teams to develop.

One was the Washington Redskins, which is you draft by position. And the other one was the Dallas Cowboys, and they were always, you take the best athlete. And I felt that that was a faulty distinction for building great cancer centers and even great football teams, and that the answer was somewhere in the middle.

Since we had all these leadership vacancies, like head of hem/onc and head of med/onc and head of neuro/onc and head of gyn/onc, deputy director.

And so, I felt we should go after the best player available for those positions, and then have that help weight the decision on which disease areas to build, with some weighting from the research that was already here.

When we got Alec Kimmelman as head of radiation oncology, and we already had Dafna Bar-Sagi and George Miller and several other people here who were RAS experts, it seemed like pancreas cancer would be an obvious area to try to build strength in.

And then we were able to get Diane Simeone [associate director, translational research] to come from Michigan, and Paul Oberstein from Columbia, to complement Deirdre Cohen, who was already here in medical oncology to fill out the team.

And then we got Kwok-Kin Wong from the Farber as head of hem/onc. We already had a good young researcher here in lung cancer.

We have a lot of lung cancer patients, who were coming to see Abe Chachoua, a great lung cancer doc. We went out and got initially Leena Gandhi, and then she was successful and went to Lilly, and we recruited Vamsidhar "Vamsi" Velcheti to be head of thoracic medical oncology. And then we went and got Robert Cerfolio from Alabama, who's a really extremely busy thoracic surgeon, robotic surgeon.

That was sort of the general strategy that we used: get the best player available for the leadership positions, and then use that to inform the areas that we're going to grow our center in.

That's actually the cancer center, not the [NCI] grant. Okay? I've always viewed grants as different from the enterprise. They are a part of the enterprise, but the grant is only a small part of the reinvigoration of the Perlmutter Cancer Center.

In terms of the grant itself, then, you have to add on additional considerations that have to do with, as you know, the vagaries of cancer center grants, like promoting collaborations, having the best cores.

And so, there I felt that doing the same thing over and over again, and expecting a different outcome is generally not a good strategy in any area of life. And this place had tried to get comprehensive status multiple times after it lost it in the '90s, and, basically, it was the same people doing it.

I felt that we needed to shake up the leadership and get a bunch of young people and new people involved, and I also felt it was important that we partner—every program have one basic scientist and one clinical person.

If you are going to have translational programs, you have to have people who are at least conversant in both areas. That was sort of the general strategy.

I don't know if that's more than you want to know, but that was the strategy...

This is terrific. I feel like I understand something. Actually, when I was calling a bunch of friends and asking, "Well, what do I ask Dr. Neel?" most of them said, "I'm not too sure what's happening at NYU." Which is sort of interesting. It's consistent with what you were saying, is that it's, they're just getting to know us. Because NYU has changed quickly.

BN: I'm starting my fifth year, but the cancer center grant went in after three years, at basically three years.

The cancer center grant went in January of last year, and that was the start of my fourth year, so I started January 2015. I would say the majority of the transformation occurred in the first three years.

It's five years ahead of when we planned to do it.

I promised the Perlmutter and the dean that we would get comprehensive status in five years, but my friend Kwok Wong, in a different context in a meeting said, "You should go big or go home."

We were, actually, lucky that we were able to fill so many of these positions and get a lot of improvement early.

And so, I felt that it was worth taking a shot at comprehensive. I felt we'd give it our best shot, and by the time we actually put the grant together and read it and everything, I felt that we deserved comprehensive status for the grant.

But I think up until then, it was a 50/50 chance. And I felt that regardless of what the site visit team said, we were a comprehensive cancer center. It was just good to get the endorsement of the site visit team that they agreed.

It kind of confirms another one of those truisms in cancer centers, which is you're as good as the people you hire.

BN: Well, that's true of any enterprise.

It seems to be.

BN: I think that another strategy that I learned is that I think there's two types of people who take leadership positions, the people who always want to be the best person in the institution, and the people who want people to be better than them around them in the institution.

I'm not intimidated by having smarter people than I am around me, and so, in fact, I think that that's the way you build strength. I mean, I had John Dick and Tak Mak back in Toronto, so I can deal with people who are better than I am.

I worked next to Lou Cantley for 20 years. If you want to see some ego destruction for a basic scientist, try that.

It's interesting, because you are in a cancer-center-rich neighborhood. Now, there are three comprehensive cancer centers in the city alone; right?

BN: Yes.

Including yours. And then two clinical. There's a basic cancer center, Cold Spring Harbor, and then, if you want to go as far as Roswell Park, there you go.

BN: Well, there is Rutgers, in New Jersey. They are a comprehensive cancer center. Rutgers is closer than Cold Spring Harbor. And Yale is not far, either.

Of course. None of it is far. I was staying within the state boundaries, but what you're saying is more realistic. Basically, does this concentration of cancer centers present any specific challenges and opportunities?

BN: I think that was definitely a challenge in terms of the grant, in terms of the committee. I think that there's a natural inclination for people to think, "Well, New York already has two comprehensive cancer centers. Why do you want a third?"

But I'll say two things about that.

One was in the context of doing the grant itself, and having to go through the catchment area exercise, it became quite clear that the catchment areas for these centers are actually quite different, and ours is clearly unique.

The other major thing that I probably should have said earlier is that the major factor that allowed us to apply for comprehensive status—and that is that something that occurred both prior to and continued through my arrival, and I take no credit for it—is the dramatic expansion of the NYU Langone Health Network.

We acquired NYU Langone Brooklyn. We have an agreement to acquire Winthrop Hospital. As of August 2019, they'll be NYU Winthrop on Long Island. And there was just a tremendous expansion of network sites all throughout Queens and, well, mainly Brooklyn and Queens, and some on Long Island.

Whereas our catchment area in 2012 and in 2007, actually, in 2001 or '02; I don't remember when, was limited to Lower Manhattan, now we serve 7.2 million lives, and our catchment area extends over four boroughs and Long Island.

Our catchment area is really that large and that deep. If you look at Mt. Sinai, Mt. Sinai really goes to Upper Manhattan, and then into Westchester, and then outward.

And then, Columbia is more on the Upper West Side and Midtown on the West Side of Manhattan, and then into Westchester, and a little bit into New Jersey. Of course, Memorial lists its catchment area as the Tri-State area, so they do overlap all of us.

But I think all of the other centers are really geographically distinct in their catchment areas. I mean, there's some overlap, obviously, but they're really quite separate.

And, of course, the other thing to keep in mind is that Brooklyn alone is four million people. It's the fourth largest city in the United States. I'm not a New Yorker, so I learned a lot about New York and about the geography and the populations and everything in doing this grant.

Whenever I talk with cancer center directors, conversation drifts to outreach and engagement these days. How is your outreach and engagement working? What's the focus?

BN: The two major weaknesses of the previous reviews were in the population sciences and in the outreach and engagement that came from there. I think that, again, antedating my arrival, the institution made a major commitment in the establishment of the Department of Population Health and the recruitment of several people into that entity, as well as the NYU Downtown campus established a new Department of Global Public Health, which also has several researchers in it who do cancer-oriented stuff.

For the grant, I think, our highest score was for community outreach and engagement, actually. And our major areas of engagement are in smoking policy, so for example, Donna Shelley and Scott Sherman have been very active in doing smoking-oriented population research that is translated into outreach into the communities to deliver best practices into, for example, New York Public Housing Projects, in terms of non-smoking policies.

There's a big e-cigarette program, both here and on the Downtown campus, in terms of evaluating the benefits and risks of e-cigarettes.

We have an Asian center at NYU Medical School, and the director of our outreach and engagement effort, Chau Trinh-Shevrin, associate director for the outreach, she's the director of that Asian center, too, and she's done a lot of work on HPV and H. pylori. And that actually nestles in very nicely with the research here, in terms of the microbiome and its contribution to tumor immunology, and also to tumor pathogenesis.

And I should say, one other area that we really do a lot of outreach into is in the obesity area.

Brian Elbel, who's also in our pop sci effort, has been instrumental in influencing legislation. He showed clearly in initial research that something so simple as putting water fountains in all the cafeterias in New York public schools reduces soda consumption. And that led to public policy changes.

We try to do that kind of outreach. And right now, we are actually in the midst of planning a big, new outreach effort that we are trying to obtain major philanthropic and grant support for that we are going to call Stamp Out Cancer Brooklyn.

We've already outlined our major strategic effort in the outreach and engagement domain for the next cycle, and it's a new program that we want to launch sometime in the next year or so.

We're trying to raise a lot of money for this.

What was the war chest? In 2015 when you came in, how much money did you think you'd have, and how much did you have?

BN: Well, I'm not really allowed to say what my startup package was, but I can say that it was north of \$100 million.

The Perlmutter gave \$51 million as part of that, and then institutional and other philanthropy was more than that.

But then that was just for my initial startup package, but the institutional commitment overall for the center in terms of new building, acquiring all these hospitals, was half a billion dollars.

Institutional commitment was about half a billion?

BN: What we listed in our institutional commitment was close to half a billion. And, again, because we acquired NYU Brooklyn, we built new centers, new clinical practices all throughout the boroughs and Long Island.

And also several new facilities here. For example, the cancer center research space more than doubled.

You've probably heard, we just announced a \$75 million anonymous gift for building a new Center for Blood Cancers. That's actually another thing that's happened here.

We had an elementary, embryonic bone marrow transplant program. There had been multiple attempts to try to get allogeneic transplants off the ground here, and it was multiple failures.

We're just really fortunate to recruit Samer Al-Homsi from Michigan State, and he's come and he's just totally transformed bone marrow transplants.

Last year, right after we got our cancer center score, we got FACT accreditation for allo. We're doing over 100 transplants this year. We're going to start a new outpatient bone marrow transplant program.

Again, I don't want to be bragging here or anything, but I think that the point I want to convey is, which again, I think is actually, unfortunately, the fact that you say it is actually validation to something I say all the time, which is I feel like in some ways Perlmutter Cancer Center is the best kept secret in New York.

I think that anything you can do to help us on that, I think that's our major limitation. People don't know it.

It's not a secret anymore. Is there anything we've missed, anything you'd like to add?

BN: No. I just want to say that I think that this is a great. I feel like the turnaround and enhancement is a great story, and I think that it's very clear that this was due to a constellation of circumstances that included most prominently the ability to convince a number of really extremely talented and productive people to leave their institutions and take the risk of coming to New York and trying to basically rebuild a now-comprehensive cancer center on the fly.

And people like Jeff Weber, and Kwok Wong, and Diane Simeone, and also Alec Kimmelman and several others—they all took a big risk by uprooting their families from major centers to come here. And I hope that they've felt validated.

Trump to dedicate \$500M over 10 years to childhood cancer

By Claire Dietz

In his State of the Union address Feb. 5, President Donald Trump said he plans to ask Congress for \$500 million over 10 years to fund pediatric cancer research—an amount Speaker of the House Nancy Pelosi (D-CA) said is insufficient.

“Many childhood cancers have not seen new therapies in decades,” Trump said. “My [president’s] budget [proposal] will ask the Congress for \$500 million over the next 10 years to fund this critical life-saving research.”

According to [Politico](#), Pelosi said in a closed-door conference meeting, “\$500 million over 10 years—are you kidding me? Who gave him that [\$50 million] figure? It’s like the cost of his protection of his Mar-a-Lago or something.”

At the same meeting, Pelosi called Trump’s proposal a “trolley ride” when compared to the Beau Biden Cancer Moonshot.

“We’re talking about a moonshot,” Pelosi said during the conference meeting Feb. 6, according to [Politico](#). “He’s talking about a trolley ride.”

In December 2016, Congress authorized \$1.8 billion over seven years for then Vice President Joe Biden’s Na-

tional Cancer Moonshot Initiative ([The Cancer Letter](#), [Dec. 16](#), 2016).

Trump’s plan would allocate \$50 million per year for childhood cancer research. For perspective, the Cancer Moonshot receives about \$257 million a year when averaged over seven years ([The Cancer Letter](#), [To the Moon](#)).

“Tonight, I am also asking you to join me in another fight that all Americans can get behind: the fight against childhood cancer,” Trump said in his address. “Joining Melania in the gallery this evening is a very brave 10-year-old girl, Grace Eline. Every birthday since she was four, Grace asked her friends to donate to St. Jude Children’s Research Hospital.

“She did not know that one day she might be a patient herself. Last year, Grace was diagnosed with brain cancer,” Trump said. “Immediately, she began radiation treatment. At the same time, she rallied her community and

raised more than \$40,000 for the fight against cancer. When Grace completed treatment last fall, her doctors and nurses cheered with tears in their eyes as she hung up a poster that read: ‘Last Day of Chemo.’ Grace—you are an inspiration to us all.”

Nancy Goodman, founder and executive director of Kids v Cancer, an advocacy group, said Trump’s speech and Pelosi’s comment, though at odds with each other, signal intent to find new money for research in pediatric cancer.

“President Trump, Speaker Pelosi, put your money where your mouth is and appropriate more than half a billion dollars to have scientists develop some cures for kids with cancer,” Goodman said to [The Cancer Letter](#). “It’s clear from President Trump’s statement and Speaker Pelosi’s statement that they’re talking about new money. So, let’s be clear about that and appropriate some new funding.”

IN BRIEF



Foundation Medicine gets genomic profiling contract from Veterans Affairs

Foundation Medicine Inc. announced a nationwide contract with the U.S. Department of Veterans Affairs National Precision Oncology Program to provide comprehensive genomic profiling for eligible Veterans with advanced cancer.

The contract covers all of Foundation Medicine's available tests, including FoundationOne CDx and FoundationOne Liquid for solid tumors, as well as FoundationOne Heme for hematologic malignancies.

"Foundation Medicine is honored to be awarded a contract to provide comprehensive genomic profiling for veterans with advanced cancer," Cindy Perettie, chief executive officer at Foundation Medicine, said in a statement. "This decision by the VA as well

as Medicare's National Coverage Determination issued in early 2018 mark important steps forward in access to personalized cancer care."

Higgins, King, Kilmer, Fitzpatrick to serve as co-chairs of House Cancer Caucus

Leading the House of Representatives Cancer Caucus are co-chairs House members Brian Higgins (D-NY), Peter King (R-NY), Derek Kilmer (D-WA), and Brian Fitzpatrick (R-PA).



Brian is a member of the House Budget Committee and the Committee on Ways & Means including its subcommittee on Health. His district includes Roswell Park Comprehensive Cancer Center.

Higgins is a founding member and co-chair of the NIH Caucus, a member of the Childhood Cancer Caucus, and an original sponsor of the Cancer Drug Parity Act.



"As a co-chair of the Cancer Caucus, I will continue to advocate for increased investment in cancer research," King said in a statement. "It is essential we continue to fight hard and provide researchers with the necessary resources."



"The Cancer Caucus is a leading voice on cancer research and funding in Congress," Fitzpatrick said in a statement. "Cancer is indiscriminate, afflicting millions of Americans each year from all walks of life."

NETRF announces \$2.5 million research grants to treat tumors

The Neuroendocrine Tumor Research Foundation announced eight new grants totaling \$2.5 million, aimed at neuroendocrine cancer research. With this newest round of funding, NETRF expands its portfolio to include research into lung neuroendocrine tumors, which affect about one in four NET patients.

The eight new projects explore some of the latest advancements in cancer:

- CAR T-cell therapy combined with antibody-drug conjugates
- Photodynamic therapy
- Deciphering the impact of mutations in key genes in NETs
- Improving outcomes by combining biomarkers and radiomics
- “Smart” chemotherapy
- Novel SSTR2 radioligands
- Alpha-particle emitting agents for the treatment of lung NETs
- Testing new cancer vaccine on NETs

NETs occur in hormone-producing cells, most commonly forming in the lung, pancreas, and gastrointestinal tract. Despite appearing in different sites, tumors forming in this cell type are classified as neuroendocrine and require different tests and treatments.

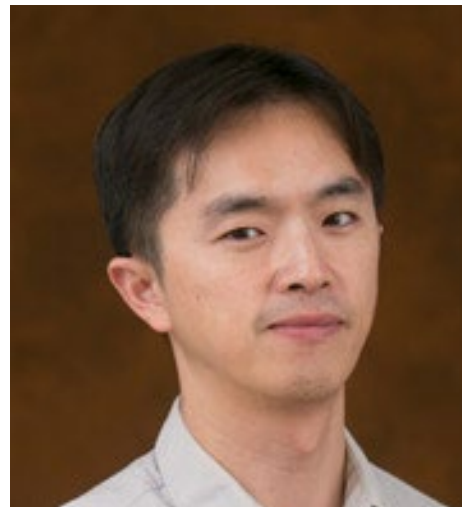
Two U.S. cancer centers will receive their first NETRF grant: Roswell Park Comprehensive Cancer Center and Moffitt Cancer Center. Two international organizations will also receive their first NETRF grant: BC Canada, Vancouver, Canada, and Radboud

University Medical Center, Nijmegen, Netherlands.

Other institutions funded in this grant cycle include the University of Pennsylvania, MD Anderson Cancer Center, Stanford University, and the University of California.

The NETRF grant process is a competitive and structured peer-review process, which starts with an annual call for letters-of-intent in late spring.

Chien-Chi Lin wins \$1.5M grant in pancreatic cancer



The School of Engineering and Technology at Indiana University–Purdue University Indianapolis said NIH has awarded a four-year R01 grant of \$1.5 million to Chien-Chi Lin, associate professor of biomedical engineering. Lin’s research is focused on pancreatic cancer.

Lin’s project, “BRAVE Hydrogels for Interrogating Cell-Matrix Interactions in Pancreatic Desmoplasia,” focuses on tumor-tissue interactions using hydrogels with engineered properties.

ADEPT System Cancer Imager wins Illinois Tech’s \$1 million Nayar Prize Competition

Illinois Institute of Technology announced a cancer imaging research team is the winner of the final round of the university’s Nayar Prize, which includes a \$500,000 personal award to team members. Including previous rounds, this brings the total amount won by this and other teams in the first Nayar Prize competition to \$1 million.

The team of Kenneth Tichauer, Illinois Tech associate professor of biomedical engineering; and Jovan Brankov, Illinois Tech associate professor of electrical and computer engineering and of biomedical engineering, and director of the Advanced X-ray Imaging Laboratory developed the Agent-Dependent Early Photon Tomography Cancer Imager with the goal of finding tumors in lymph nodes of breast cancer patients at earlier stages.

The ADEPT System Cancer Imager dyes the entire lymph node, as opposed to a small sample. The combination of the special dyeing process and camera improvements provides a sharper picture of the tissue sample at the molecular level.

The result is a system that allows pathologists to find smaller tumors and prescribe a precise and personalized drug treatment for the patient. Team members estimate 40,000 more women will be properly diagnosed annually using the ADEPT imager.

The team is planning a clinical trial of the ADEPT system, in a partnership with Sanford Research in Sioux Falls, South Dakota, and the University of Chicago Department of Pathology.

The ADEPT Cancer Imager team was selected as one of three finalists for the inaugural Nayar Prize when the competition was announced in 2015, earning \$100,000 to continue its research. It was selected from that pool as the sole phase II finalist, earning an additional \$200,000 for further research. The team members can use the final, personal \$500,000 award at their discretion with no restrictions.

Team members include Miles Wernick, Motorola Endowed Chair Professor of Electrical and Computer Engineering, director of the Medical Imaging Research Center and professor of biomedical engineering; Lori Andrews, distinguished professor of law and director of the Institute for Science, Law, and Technology at Chicago-Kent College of Law; and Yongyi Yang, Harris Perlstein Professor of Electrical and Computer Engineering and professor of biomedical engineering.

Christiana's Boman receives \$900K grant for stem cell research



Bruce Boman, senior research scientist, at the Helen F. Graham Cancer Center & Research Institute of Christiana Care Health System, has received a \$917,000

grant award from the Lisa Dean Moseley Foundation to further stem cell research into the origins of colon cancer.

The three-year grant will enable Boman and his team at the Center for Translational Cancer Research at Christiana Care to continue building on their discovery that stem cell overpopulation is the mechanism that drives cancer development and growth in the colon.

Boman's team will take a multidisciplinary approach drawn from tumor biology, cancer genetics, pathology, medical oncology and molecular biology to discover how stem cells are regulated in the normal healthy colon and how gene mutations contribute to stem cell overpopulation in tumors.

Specifically, they will study how inactivation of the adenomatous polyposis coli tumor suppressor gene leads to stem cell overpopulation that drives colon cancer development and growth.

Earlier this year, Boman published findings that the retinoic acid signaling pathway acts to induce differentiation of colon cancer stem cells and reduce cancer stem cell overpopulation. Boman's findings suggest that treatment with retinoid drugs, which are derived from vitamin A, could provide a therapeutic strategy to selectively target cancer stem cells and decrease the number of highly resistant cancer cells.

Conventional research over the last 50 years has been that tumors undergo a series of genetic mutations that lead to the unchecked growth of tumors and their progression to metastatic cancer. Traditional therapies designed to kill the bulk of cancer tumor cells continue to fall short of a cure for advanced, drug resistant colon cancers.

"Our thinking has shifted to the insight that cancers originate in tissue stem cells through dysregulation or mal-

function of the self-renewal process and that cancer stem cells drive tumor growth," Boman said in a statement. "It follows that the optimal way to treat cancer (especially advanced cancer) is to eliminate cancer stem cells."

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Study finds HIV+ cancer patients benefit from immunotherapy

Researchers at Georgetown Lombardi Comprehensive Cancer Center released a study that may show immunotherapy offers similar benefit to cancer patients living with HIV.

The study, published in *JAMA Oncology*, focused on whether a relatively new class of drugs called checkpoint inhibitors is both safe and effective in patients with advanced cancer who also live with HIV. Because checkpoint inhibitors manipulate the immune system, the concern has been that these therapies might have adverse effects such as virus reactivation in patients with HIV infection.

Investigators searched the medical literature to find 73 HIV patients whose cancer had been treated with check-

point inhibitors. Only a fraction of patients came from a clinical trial; the rest were mostly case reports and case series from oncologists who chose to treat their patients with cancer and HIV infection with the new cancer drugs.

“Cancer patients with HIV and their oncologists have found themselves in a real conundrum,” the study’s lead investigator Chul Kim, assistant professor at Georgetown Lombardi, attending physician at MedStar Georgetown University Hospital and MedStar Washington Hospital Center, said in a statement. “Because of their HIV infection, they are at higher risk of developing cancer than people who are not infected.”

“In fact, cancer has become one of the leading causes of death in patients with HIV,” Kim said. “But conventional chemotherapies can reverse HIV suppression, and on top of that, these patients are widely excluded from clinical studies that test the next generation of cancer treatments.”

“We hope our finding will lead to increased study of checkpoint inhibitors in patients with HIV and cancer,” says Kim. He adds the checkpoint inhibitors might not just keep cancer in check. “There are signals in this analysis and other studies that suggest these new cancer drugs may restore an immune response against HIV in patients whose immune system is exhausted by its long fight with HIV.”

Kim and co-author, Michael Cook, internal medicine resident at MedStar Georgetown University Hospital, found that checkpoint inhibitors offered similar objective response rates

in treating non-small cell lung cancer (30 percent) and melanoma (27 percent) as has been found in non-infected cancer patients.

Additionally, the inhibitor offered benefit in treatment of Kaposi’s sarcoma, a cancer strongly linked to HIV infection for which there are not many effective treatment options. The objective response in this patient population was 67 percent.

HIV patients did not experience increased side effects, compared to the norm, and HIV remained undetectable in 93 percent of patients (26 of 28) known to have undetectable viral load before treatment.

“And we found something that is really intriguing,” Kim said. “In six patients who had a detectable load of HIV in the blood before treatment, five had a decrease in their viral load after treatment. It could be that checkpoint inhibitors are helping to suppress HIV, though this finding needs to be verified in future studies.”

To further investigate these findings, Georgetown plans to launch a clinical trial to test checkpoint inhibitor therapy as first-line therapy in lung cancer patients with HIV or viral hepatitis.

High-dose radiation therapy improves long-term survival in stage IV cancers

The first report from a phase II, multi-center clinical trial indicates

that a newer, more aggressive form of radiation therapy, stereotactic radiation, can extend long-term survival for some patients with stage-IV cancers while maintaining their quality of life.

The study is published in the January issue of *International Journal of Radiation Oncology · Biology · Physics* (Red Journal), the flagship scientific journal of the American Society for Radiation Oncology.

“Despite many advances in cancer care over the last 20 to 30 years, some patients still go on to develop metastatic or stage-IV disease,” said Dwight Heron, senior author of the study and director of radiation services at UPMC Hillman Cancer Center in Pittsburgh. “Generally speaking, radiation therapy in that setting has been used only to make the patient comfortable.

“It also has been the case, however, that a small number of patients with stage-IV disease could have surgery to remove their metastases and live a long time,” Heron said. “And so our question was, could we use highly focused radiation to destroy those tumors and have the same effect as surgery? The initial answer from this large prospective trial is yes.”

Patients in the trial were treated with stereotactic radiation. Increasing evidence points to stereotactic radiation as a viable alternative when patients cannot undergo surgery to remove metastatic tumors.

“With stereotactic radiation, we use a different type of highly precise local therapy to target tumors in the lungs, liver, bones or kidneys with precision that is analogous to surgery, and with very few side effects or harm to the patient’s quality of life,” said Heron.

In this phase II trial, Heron and his colleagues enrolled 147 patients across three large cancer centers to evaluate

the safety and feasibility of stereotactic radiation for a variety of oligometastatic cancers. Each patient had up to five metastases—most had either one (71%) or two (19%)—in one to three new sites. The metastases were located most commonly in the lung (52%), followed by lymph nodes (16.5%), bone (15%) or liver (7%).

All patients received stereotactic radiation to all metastatic sites. Radiation dosing and fractionation were dependent on the size and location of each metastasis. All patients had good performance status (ECOG 0-1) and a life expectancy of more than 6 months. Median follow-up time for this report was 41 months (range=14.6-59.0).

Following treatment with stereotactic radiation, more than eight in ten patients (84%) survived at least 1 year, and four in ten (43%) survived 5 years or longer. The median overall survival time was 42.3 months.

Local recurrences were uncommon; half of the patients experienced complete (26%) or partial (26%) remission following treatment. An additional third (32%) had stable disease, meaning their cancer did not progress or recede.

The remaining patients either had local progression following treatment (14%) or their response could not be determined (12%). Distant recurrences were more common, with a median time of 8.7 months until distant progression. The one-year and five-year rates of distant progression free survival were 44 percent and 17 percent, respectively.

The type of primary tumor was associated with both OS ($p=0.002$) and DPFS ($p=0.008$). Patients with primary breast (9% of patients), prostate (7.5%) and colorectal (21%) tumors had longer survival than those with primary lung (22%) or head and neck (11%) tumors.

A unique aspect of the trial design was the decision to use patient-reported rather than physician-assessed quality of life. Patients reported no significant changes in their quality of life immediately after completing stereotactic radiation, nor at 6 weeks, 3 months and 9 months follow-up. At the 6- and 12-month marks, QoL was significantly better than before treatment.

Heron said his team plans to continue enrolling patients into the trial, with a goal of expanding the current 147 patients to roughly 200 total patients. Moving forward with additional trials, they also will look at treating patients with larger numbers of metastatic lesions and combining stereotactic radiation with emerging treatments such as immunotherapy.

This trial adds to the growing body of evidence supporting the use of stereotactic radiation for oligometastatic cancers. Two randomized, phase II trials presented at the most recent ASTRO Annual Meeting, for example, also found the treatment may lengthen survival, sometimes dramatically, for patients with stage-IV disease. If validated through larger randomized trials, radiation therapy could be utilized as a safe and effective approach to improve outcomes for patients with cancers that have begun to spread throughout the body.

Combination of Veyonda/ radiotherapy delivers clinical benefits

Noxopharm announced interim results from the dose-ranging component of the DARRT-1 study. Some of their key findings include combining Veyonda with low-dose radiotherapy applied to a single metastasis is able to produce an anti-cancer response

in both the irradiated and non-irradiated lesions as evidenced by PSA response, pain reduction, and/or tumour measurements.

A dose-response was observed, with the 1200 mg dose confirmed as the therapeutic dose. Clinical responses were achieved with no serious side-effects related to Veyonda, the company said.

The DARRT treatment regimen involves using Veyonda to trigger a generalised anti-cancer response to radiotherapy against cancer cells throughout the body. This is known as an abscopal response and is thought to involve a generalised immune response.

Veyonda has been shown to activate the body's innate immune system, an action that the company believes will provide a transformative approach to the use of radiotherapy in oncology, enabling low dosages of focused radiation to be used to create a generalised anti-cancer effect.

The company's ultimate goal in prostate cancer is to evaluate the DARRT treatment regimen across the full spectrum of prostate cancer from early-stage to late-stage. The DARRT-1 study is the starting point in this program involving end-stage prostate cancer.

The tumor burden in stage IV prostate cancer generally is greatest in the skeleton and is associated with significant pain. Treatment in these men nearing end of life is palliative, with pain relief a major objective through the use of radiotherapy and pain medications.

NOX is developing the DARRT regimen in advanced prostate cancer with the dual objectives of providing better palliation (pain relief) and extending survival and doing so in a well-tolerated way.

The DARRT-1 study has two stages. Stage I involving 12 patients was designed to provide an indication of the benefit:risk profile of three different doses of Veyonda (400, 800, 1200 mg daily) including four patient per dose. Patients included in this phase were required to have at least one soft tissue lesion that was amenable to accurate radiographic measurement (according to RECIST 1.1).

Stage II involved expansion into an additional 12 patients at a dose selected by an independent data safety monitoring board. As previously announced, stage II of the trial was initiated at the 1200 mg dose following DSMB review of the 6-week data.

Stage II includes patients who lack a soft tissue lesion and whose lesion requiring radiotherapy is located in the bone, which often cannot be accurately measured (according to RECIST 1.1).

Determination of a generalised response in such patients will be on the basis of PSA and pain responses. The final 4 patients in this stage have been screened and the study is expected to be fully enrolled within 2 weeks.

All three doses were well tolerated and no serious side-effects were reported as being related to Veyonda. For patients with advanced disease receiving palliative therapy, not doing any harm is a key factor in any new treatment to be introduced, and Veyonda is looking increasingly as meeting this fundamental need.

Efficacy: Efficacy analyses include reported changes from baseline (Day 1 of the study) at 12- and 24-weeks following radiotherapy on three key measures: PSA levels, pain levels, and aggregate lesion sizes.

Falls in PSA of >50% compared to baseline and reductions in pain severity of >30% compared to baseline are consid-

ered to be significant biochemical/tumour and pain responses respectively.

Apart from pain relief in 2 patients in the 400 mg cohort, this dose did not appear to have any significant anti-cancer effect in this small number of patients.

Efficacy signals were demonstrated in the 800 and 1200 mg cohorts at 12 weeks. Two patients in each cohort had PSA falls > 50% (51-78%). 3/4 patients in the 800 mg cohort and 2/4 patients in the 1200 mg cohort had a pain response of > 30% (52-92%), the company said.

One patient in the 800 mg cohort had a reduction in aggregate tumour diameter of > 30% (RECIST 1.1 partial response); the other three 800 mg patients and 3 of the 1200 mg patients were classified by RECIST 1.1 as having stable disease at 12-weeks.

The changes in PSA levels and total tumour lengths, relative to starting levels across all 11 evaluable stage I patients.

Veyonda (previously known as NOX66) is a dosage formulation of the experimental anti-cancer drug, idronoxil, developed specifically to preserve the anti-cancer activity of idronoxil in the body and to enhance its drug-like behaviour.

Idronoxil inhibits the oncogene, Ecto-NOX disulfide-thiol exchanger type 2, leading to inhibition of the key secondary pro-survival messenger, sphingosine-1-phosphate. This enhances the DNA-damaging effects of radiotherapy and cytotoxic chemotherapy, as well as activating the body's innate immune system.

The DARRT (Direct and Abscopal Response to Radiotherapy) Program is testing the ability of Veyonda to increase tumour response to palliative dosages of radiotherapy. The DARRT treatment regimen entails a 5-day

course of radiotherapy (20-30 Gy) in 5 fractionated dosages targeting a single tumour, and the Veyonda administered daily for up to 3 weeks.

The rationale of DARRT is to combine the radio-enhancing properties of Veyonda that stem from its inhibition of sphingosine-1-phosphate pro-survival functions, combined with its ability to stimulate the body's first line immune defence cells against cancer.

The clinical outcome being sought is greater shrinkage of irradiated tumours and shrinkage of all non-irradiated tumours. The DARRT treatment regimen is being tested initially in prostate cancer, but in due course is to be extended into other forms of solid cancer that the Company believes will assist the Veyonda marketing approval process.

DARRT-1 is a phase Ib 24-subject study being conducted in Georgia and Australia. The study is in 2 stages, each of 12 subjects. Stage I is dose-finding entailing 3 cohorts of 4 subjects receiving 400 mg, 800 mg and 1200 mg Veyonda respectively. In stage II, the 12 subjects are receiving the 1200 mg Veyonda dose. The subjects are being assessed clinically at 6-, 12- and 24- weeks.

Prolonged time sitting shown to increase risk of colorectal cancer

A study in *JNCI Cancer Spectrum* has identified a connection between prolonged time spent sitting while watching TV and an increased risk of colorectal cancer for younger Americans.

Young-onset colorectal cancer, diagnosed under age 50, is increasing in the U.S. and globally, sharply contrasting with the dramatic decreases among

older people, largely as a result of cancer screening initiatives.

Young-onset colorectal cancer has potentially different molecular characteristics compared to those of late-onset, and is typically more aggressive and found at a more advanced stage than those in older patients, resulting in greater years of life lost. Despite these trends, researchers have identified few risk factors specific to young-onset colorectal cancer.

Researchers here studied sedentary TV reviewing time, as well as other sedentary behaviors, in 89,278 American women in the Nurses' Health Study II. Of the 118 cases of young-onset colorectal cancer diagnosed over two decades of follow up, more than one hour of daily TV viewing time was associated with a 12% increase in risk compared to those who watched less.

The results were even more striking for those watching more than two hours/day with a nearly 70% increase in risk. This association was independent of BMI and exercise and was consistently observed among women without a family history of colorectal cancer. The association was also more pronounced for rectal cancer compared to colon cancer.

These findings are among the first to link specific sedentary behavioral patterns with risk of young-onset colorectal cancer. "This study may help identify those at high risk and who might benefit more from early screening," said Yin Cao, assistant professor of surgery at Washington University School of Medicine, and the study's co-senior author. "The fact that these results were independent of BMI and physical activity suggests that being sedentary may be an altogether distinct risk factor for young-onset colorectal cancer."

DRUGS & TARGETS



FDA approves therapy for adult patients with blood clotting disorder

FDA has approved Cablivi (caplacizumab-yhdp) injection in combination with plasma exchange and immunosuppressive therapy, for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura.

The FDA granted the approval to Ablynx.

"Patients with aTTP endure hours of treatment with daily plasma exchange, which requires being attached to a machine that takes blood out of the body and mixes it with donated plasma and then returns it to the body. Even after days or weeks of this treatment, as well as taking drugs that suppress the immune system, many patients will have a recurrence of aTTP," Richard Pazdur, director of the FDA's Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products, said in a statement. "Cablivi is the first targeted treatment that inhibits the formation of blood clots. It provides a new treatment option for patients that may reduce recurrences."

Cablivi was studied in a clinical trial of 145 patients who were randomized to re-

ceive either Cablivi or a placebo. Patients in both groups received the current standard of care of plasma exchange and immunosuppressive therapy.

The results of the trial demonstrated that platelet counts improved faster among patients treated with Cablivi, compared to placebo. Treatment with Cablivi also resulted in a lower total number of patients with either aTTP-related death and recurrence of aTTP during the treatment period, or at least one treatment-emergent major thrombotic event.

The proportion of patients with a recurrence of aTTP in the overall study period (the drug treatment period plus a 28-day follow-up period after discontinuation of drug treatment) was lower in the Cablivi group (13 percent) compared to the placebo group (38 percent), a finding that was statistically significant.

The FDA granted this application Priority Review designation. Cablivi also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

Pfizer given positive CHMP opinion for Vizimpro in NSCLC

The Committee for Medicinal Products for Human Use of the European Medicines Agency has adopted a positive opinion recommending Vizimpro (dacomitinib) 45 mg, as monotherapy, be granted marketing authorization in the European Union for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with epidermal growth factor receptor-activating mutations. The CHMP's opinion will now be reviewed by the European Commission

The agent is sponsored by Pfizer.

Vizimpro was approved by FDA in 2018 for the first-line treatment of patients

with metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test. It was also recently approved in Japan for EGFR gene mutation-positive, inoperable or recurrent NSCLC.

The Marketing Authorization Application for Vizimpro was based on results from ARCHER 1050, a randomized, multicenter, multinational, open-label, phase III study conducted in patients with locally advanced unresectable, or metastatic NSCLC harboring EGFR exon 19 deletion or exon 21 L858R substitution mutations, an Eastern Cooperative Oncology Group performance status of 0 or 1; with no prior therapy for metastatic disease or recurrent disease with a minimum of 12 months disease-free after completion of systemic therapy. A total of 452 patients were randomized 1:1 to Vizimpro 45 mg (n=227) or gefitinib 250 mg (n=225).

Vizimpro is an oral, once-daily, irreversible pan-human epidermal growth factor receptor kinase inhibitor for first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with epidermal growth factor receptor-activating mutations.

Vizimpro is approved in the U.S. for the first-line treatment of patients with metastatic non-small cell lung cancer with epidermal growth factor receptor exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test. Vizimpro is also approved in Japan for EGFR gene mutation-positive, inoperable or recurrent NSCLC. The applications in the US and Japan were reviewed and approved under the Priority Review program.

In 2012, Pfizer and SFJ Pharmaceuticals entered into a collaborative development agreement to conduct ARCHER 1050 across multiple sites. SFJ is a global drug development company, which provides a unique and highly customized co-development partnering model for the world's top pharmaceutical

and biotechnology companies. Under the terms of this agreement, SFJ Pharmaceuticals provided the funding and conducted the trial to generate the clinical data used to support this application. Pfizer retains all rights to commercialize Vizimpro globally.

The efficacy of Vizimpro was demonstrated in ARCHER 1050, a global phase III head-to-head trial conducted in patients with locally advanced unresectable, or metastatic non-small cell lung cancer harboring epidermal growth factor receptor exon 19 deletion or exon 21 L858R substitution mutations, with no prior therapy for metastatic disease or recurrent disease with a minimum of 12 months disease-free after completion of systemic therapy.

A total of 452 patients were randomized 1:1 to Vizimpro 45 mg (n=227) or gefitinib 250 mg (n=225). Randomization was stratified by region and EGFR mutation status. The primary endpoint of the study was progression-free survival as determined by blinded Independent Radiology Central review. Key secondary endpoints included objective response rate, duration of response, overall survival, and patient-reported outcomes.

Genentech submits sBLA for Kadcylla for breast cancer

Genentech has submitted a supplemental Biologics License Application to the FDA for Kadcylla (ado-trastuzumab emtansine) for adjuvant treatment of people with HER2-positive early breast cancer with residual disease after neo-adjuvant treatment.

Genentech is a member of the Roche Group.

The FDA is reviewing the application under the Real-Time Oncology Review and Assessment Aid pilot programs, which aim to explore a more efficient

review process to ensure safe and effective treatments are available to patients as early as possible.

For this indication, Kadcyła was also granted Breakthrough Therapy Designation, which is designed to expedite the development and review of medicines intended to treat serious or life-threatening diseases.

This application is based on results of the phase III KATHERINE study showing Kadcyła significantly reduced the risk of invasive breast cancer recurrence or death from any cause (invasive disease-free survival) by 50 percent (HR=0.50, 95% CI 0.39-0.64, $p < 0.0001$) compared to Herceptin (trastuzumab) as an adjuvant treatment in people with HER2-positive EBC who have residual disease present following neoadjuvant treatment.

People who have residual disease after neoadjuvant treatment have a worse prognosis than those with no detectable disease. At three years, 88.3 percent of people treated with Kadcyła did not have their breast cancer return compared to 77.0 percent treated with Herceptin, an absolute improvement of 11.3 percent.

KATHERINE is an international, multi-center, two-arm, randomized, open-label, Phase III study evaluating the efficacy and safety of Kadcyła versus Herceptin as an adjuvant therapy in people with HER2-positive EBC who have pathological invasive residual disease in the breast and/or axillary lymph nodes following neoadjuvant therapy that included Herceptin and taxane-based chemotherapy.

The primary endpoint of the study is iDFS, which in this study is defined as the time from randomization free from invasive breast cancer recurrence or death from any cause. Secondary endpoints include disease-free survival and overall survival.

Kadcyła is an antibody-drug conjugate engineered to deliver potent chemo-

therapy directly to HER2-positive cells. It is designed to limit damage to healthy tissues, although it can still affect them. Kadcyła can cause serious side effects.

It combines two anti-cancer agents using a stable linker: the HER2-targeting trastuzumab (the active ingredient in Herceptin) and the chemotherapy agent DM1. Kadcyła is the only ADC approved for the treatment of HER2-positive metastatic breast cancer. In the U.S., Genentech licenses technology for Kadcyła under an agreement with ImmunoGen, Inc.

Kadcyła, as a single agent, is indicated for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy.

Merck KGaA and GSK to co-develop immunotherapy M7824

Merck KGaA and GSK have agreed to jointly develop and commercialize M7824 (bintrafusp alfa). M7824 is an investigational bifunctional fusion protein immunotherapy that is currently in clinical development, including potential registration studies, for multiple difficult-to-treat cancers.

This deal includes a phase II trial to investigate M7824 compared with pembrolizumab as a first-line treatment in patients with PD-L1 expressing advanced NSCLC.

M7824 is designed to simultaneously target two immuno-suppressive pathways, transforming growth factor- β trap and an anti-programmed cell

death ligand-1, that are commonly used by cancer cells to evade the immune system. Bifunctional antibodies aim to increase efficacy above and beyond that achieved with individual therapies or combinations of individual therapies. M7824 has the potential to offer new ways to fight difficult-to-treat cancers beyond the established PD-1/PD-L1 class. In addition to use as a single agent, M7824 is also being considered for use in combination with other assets from the pipelines of both companies.

Merck KGaA will receive an upfront payment of €300 million and is eligible for potential development milestone payments of up to €500 million triggered by data from the M7824 lung cancer program.

Merck KGaA will also be eligible for further payments upon successfully achieving future approval and commercial milestones of up to €2.9 billion. The total potential deal value is up to €3.7 billion. Both companies will jointly conduct development and commercialization with all profits and costs from the collaboration being shared equally on a global basis.

Bintrafusp alfa is the proposed International Nonproprietary Name for the bifunctional immunotherapy M7824. Bintrafusp alfa is currently under clinical investigation and not approved for any use anywhere in the world.

M7824 is an investigational bifunctional immunotherapy that is designed to combine a TGF- β trap with the anti-PD-L1 mechanism in one fusion protein. M7824 is designed to combine co-localized blocking of the two immuno-suppressive pathways—targeting both pathways aims to control tumor growth by potentially restoring and enhancing anti-tumor responses.

M7824 is currently in phase I studies for solid tumors, as well as a randomized phase II trial to investigate M7824 compared with pembrolizumab as a first-line treatment in patients with PD-L1

expressing advanced NSCLC. The multicenter, randomized, open-label, controlled study is evaluating the safety and efficacy of M7824 versus pembrolizumab as a monotherapy treatment.

To-date, nearly 700 patients have been treated with M7824 across more than 10 tumor types in phase I studies. Encouraging data from the ongoing phase I studies indicates M7824's potential safety and clinical anti-tumor activity across multiple types of difficult-to-treat cancers, including advanced NSCLC, human papillomavirus-associated cancers, biliary tract carcinoma and gastric cancer.

In addition, in pre-clinical studies M7824 demonstrated superior anti-tumor activity, compared with anti-PD-L1 alone or with anti-PD-L1 and TGF- β trap when co-administered. In total, eight high priority immuno-oncology clinical development studies are ongoing or expected to commence in 2019, including studies in NSCLC and biliary tract cancers.

FDA pursues order to bar some retailers from selling tobacco in efforts to target tobacco use by minors

FDA has initiated enforcement action against several retail locations of Walgreen Co. and Circle K Stores Inc. for repeated violations of restrictions on the sale and distribution of tobacco products, including sales of cigars and menthol cigarettes to minors.

The agency filed complaints seeking No-Tobacco-Sale Orders, which seek to bar the two retail locations from selling tobacco products for 30 days. The two retail outlets that are the subject of these NTSO actions are a Walgreens store in Miami and a Circle K store in Charleston, South Carolina.

Notably, Walgreens is currently the top violator among pharmacies that sell tobacco products, with 22 percent of the stores inspected having illegally sold tobacco products to minors.

FDA Commissioner Scott Gottlieb said he will request a meeting with corporate management of Walgreens to "discuss whether there is a corporate-wide issue related to their stores' non-compliance."

"[I will] put them on notice that the FDA is considering additional enforcement avenues to address their record of violative tobacco sales to youth," FDA Commissioner Scott Gottlieb, said in a statement. "I'm also deeply disturbed that a single pharmacy chain racked up almost 1,800 violations for selling tobacco products to minors across the country."

An estimated 4.9 million middle and high school students reported current (past 30 days) use of any tobacco product in 2018, according to preliminary results of the 2018 National Youth Tobacco Survey.

An "epidemic-level rise" in e-cigarette use over the last year has led overall tobacco product use to increase by 38 percent among high school students (to 27.1 percent) and by 29 percent among middle school students (to 7.2 percent) in the last year, reversing the declines seen in the last few years, the survey said.

The NTSO action against this Walgreens outlet follows the issuance of more than 1,550 warning letters and 240 civil money penalty actions against Walgreens stores nationwide for unlawful tobacco product sales to minors. This is, however, the first NTSO action taken against a Walgreens store.

While the NTSO action against Circle K is not its first, it marks the first time the agency has initiated an NTSO complaint for the sale of deemed products (cigars) to minors. Since 2010, the FDA has issued over 1,045 warning letters and 205 civil money penalty actions to retailers doing business as Circle K for sales to minors.

Retailers who receive an NTSO complaint from the FDA may enter into a settlement agreement or respond with an answer and contest the allegations before an administrative law judge. If an NTSO goes into effect, a retailer is responsible for ensuring that the establishment does not sell tobacco products during the specified period.

FDA said it plans to conduct unannounced compliance check inspections during that period to check whether each establishment is complying with the terms of the order and will take further action if necessary.

NCI TRIALS



NCI Trials for February

The National Cancer Institute Cancer Therapy Evaluation Program approved the following clinical research studies last month.

For further information, contact the principal investigator listed.

Phase I NRG-LU004

Phase I Trial of Accelerated or Conventionally Fractionated Radiotherapy Combined with MEDI4736 (Durvalumab) in PD-L1 High Locally Advanced Non-Small Cell Lung Cancer (NS-CLC) (ARCHON-1)

NRG Oncology
Lin, Steven H.
(713) 563-8490

Phase I/II 10200

Combination Pinometostat and 5-Azacitidine for the Treatment of Patients with Relapsed / Refractory Acute Myeloid Leukemia, or Newly Diagnosed Patients who are Ineligible for or Unwilling to Undergo Intensive Therapy, who Harbor an 11q23 Rearrangement

JHU Sidney Kimmel Comprehensive Cancer Center LAO
Stein, Eytan M.
(212) 639-3314

Phase I/II 10212

A Phase 1b/2 Study of Pinometostat in Combination with Standard Induction Chemotherapy in Newly Diagnosed Acute Myeloid Leukemia with MLL Rearrangement

Ohio State University Comprehensive Cancer Center LAO
Blachly, James Stewart
(614) 685-5667

Phase I/II EAA172

Phase 1/2 Study of Daratumumab, Bortezomib, Dexamethasone with or Without Venetoclax in Relapsed/Refractory Multiple Myeloma with Assessment for t(11;14) Status

ECOG-ACRIN Cancer Research Group
Thompson, Michael A.
(414) 219-4763

Phase II 10181

A Phase 2 Study of Savolitinib in Subjects with MET Amplified Metastatic Colorectal Cancer

Duke University - Duke Cancer Institute LAO
Strickler, John Howard
(919) 681-6006

Phase II ANBL17P1

A Pilot Induction Regimen Incorporating Chimeric 14.18 Antibody (ch14.18, dinutuximab) (NSC# 764038, IND# 4308) and Sargramostim (GM-CSF) for the Treatment of Newly Diagnosed High-Risk Neuroblastoma

Children's Oncology Group
Federico, Sara Michele
(901) 595-7942

Phase II EAQ171CD

Implementing a Virtual Tobacco Treatment in Community Oncology Practices: "Smoke Free Support Study 2.0"

ECOG-ACRIN Cancer Research Group
Park, Elyse
(617) 724-6836

Phase II S1900A

A Phase II Study of Rucaparib in Patients with Genomic LOH High and/or Deleterious BRCA1/2 Mutation Stage IV or Recurrent Non-Small Cell Lung Cancer (LUNG-MAP Sub-Study)

SWOG
Riess, Jonathan W.
(916) 734-3772

Phase II/III A041701

A Randomized Phase II/III Study of Conventional Chemotherapy +/- Uproleselan (GMI-1271) in Older Adults with Acute Myeloid Leukemia Receiving Intensive Induction Chemotherapy

Alliance for Clinical Trials in Oncology
Uy, Geoffrey L.
(314) 747-8439

Phase Other AEWS18B3-Q

Identifying Inherited Germline Variation Associated with Ewing Sarcoma Risk

Children's Oncology Group
Machiela, Mitchell
(240) 760-6518

Phase Other AHOD18B2-Q

Identifying Treatment Response Predictors in Pediatric Hodgkin Lymphoma; A Validation Set for AHOD12B2

Children's Oncology Group
Horton, Terzah M.
(832) 824-4269

Phase Other AREN18B5-Q

Genomic Analysis of Bilateral Wilms Tumor

Children's Oncology Group
Murphy, Andrew Jackson
(901) 930-5205

Phase Other S1800NMIO

A LUNG-MAP Version Control Protocol for Non-Matched Immunotherapy Sub-Studies

SWOG
Papadimitrakopoulou, Vassiliki A.
(713) 792-6363

Phase Other S1900BDSS

A Lung-MAP Version Control Protocol for Biomarker-Driven Sub-Studies

SWOG
Papadimitrakopoulou, Vassiliki A.
(713) 792-6363

Phase Other URCC-18004CD

Understanding the Impact of Drug Shortages on Oncology Care Delivery

University of Rochester NCORP Research Base
Hill, Elaine
(585) 275-0165