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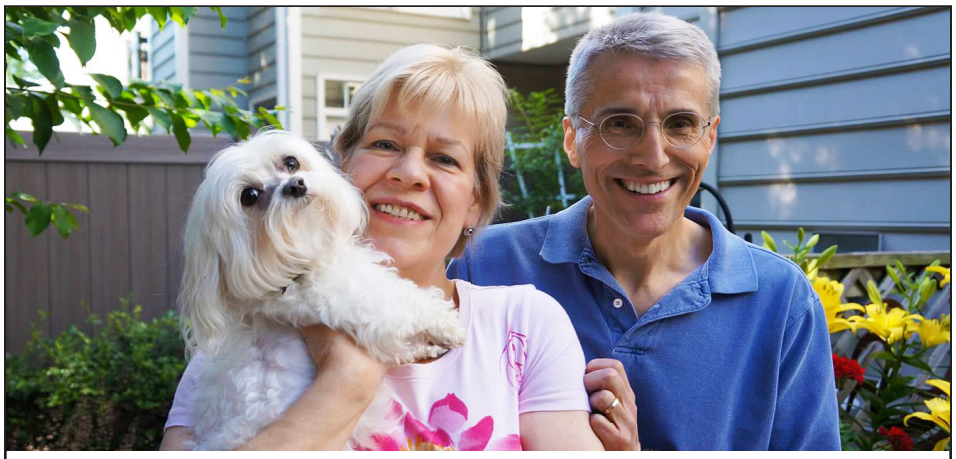

The Pazdurs in their garden in Bethesda, with their dog, Cleo. The dog's full name is Cleopatra, Queen of Denial.

Mary Pazdur, 63, Dies of Cancer; What Her Husband Has Learned

By Paul Goldberg

The job interview wouldn't last more than 15 minutes, Richard Pazdur believed.

So, on a June morning in 1999, his wife Mary settled down to wait at a restaurant near the FDA buildings alongside Rockville Pike.

The restaurant turned out to be Hooters, and Mary ended up spending three hours at the joint known for all-you-can-eat chicken wings served by scantily clad waitresses known as Hooters Girls.

"How much Hooters coffee can you drink?" Mary said frequently, retelling the story of her introduction to FDA, Washington and cancer politics.

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Rick's Search for Meaning

On Nov. 17, Richard Pazdur, director at the FDA Office of Hematology and Oncology Products, spoke about the role that has been thrust upon him: that of a "regulator/advocate."

(Continued to page 6)

NCI Director's Report

Lowy: Higher RPG Success Rates in 2015; Continuing Resolutions Will Slow Progress

NCI awarded about 635 R01s in 2015, up from 629 in 2014, said NCI Acting Director Doug Lowy at a recent joint meeting of the National Cancer Advisory Board and the NCI Board of Scientific Advisors.

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Richard Pazdur Says Wife's Illness Made Him an Advocate

(Continued from page 1)

Rick got the job, and over 16 years, he shaped the FDA approach to drug approval, setting forth a set of criteria accepted by drug companies, academics and NCI. Mary was by his side, supportive, practical, compassionate, intuitive, and intolerant of nonsense. For most of these 16 years, she was an oncology nurse practitioner at the NIH Clinical Center. She eventually took the therapies she had worked on.

Mary died of ovarian cancer Nov. 24. She was 63.

Her death and the three-year struggle that preceded it appears to have launched Rick, director of the Office of Hematology and Oncology Products in the FDA Center for Drug Evaluation and Research, into a new career phase, one where he infuses an advocate's urgency into his unchallenged power—he's the closest thing America has to a cancer czar.

"This three-year period of time has given us the opportunity for observation of the healthcare system from the other side of the stethoscope," Pazdur said Nov. 17, at a Washington conference sponsored by Friends of Cancer Research. "You see the worst of the system; you see the fact that you're not immune just because you're a doctor or a member of a doctor's family."

At the time Rick uttered these words, Mary was at the Casey House of the Montgomery County Hospice.

The FOCR talk—an onstage conversation with the group's chair and founder Ellen Sigal—is posted here.

A few weeks earlier, the Pazdurs sat down for a chat with Ellen Stovall, senior health policy advisor with the National Coalition for Cancer Survivorship. The hour-long interview, filmed at the Pazdurs' house in Bethesda, is posted here. A shorter version was published on the NCCS website and in the Oct. 23 issue of The Cancer Letter.

The two conversations address the FDA approval criteria, accrual to studies, reporting of toxicities, difficulties of getting treatments on compassionate basis, and the need to complete consolidation of the FDA oncology functions.

Sigal appears to have launched the buzzword "integration" to describe this proposed reorganization of FDA. As it is, Pazdur's office doesn't regulate cancer vaccines, cellular therapies, assays and devices.

The conversations also depict the couple's coming to terms—publicly—with impending loss. And they record oncology's principal rainmaker adopt the language of advocacy.

Consider this statement, made in his conversation with Sigal:

"I have morphed from 'the regulator' to the unique position of 'regulator/advocate.'

"What we're seeing now is not a patient voice but a patient cry—wanting to have their position heard.

"The position of a patient should be defined by the patient—not by somebody else. Certainly not by the FDA, and not by the pharmaceutical industry nor the clinical trial enterprise—a multi-billion dollar enterprise. Rather than the patients being asked to come and comment about a predefined issue, patients need to direct the show.

"So the question I have for the patients is 'what do you want?' You need to run the show—not the FDA, not the NCI, and not the pharmaceutical companies. Ultimately, the clinical trials are about you."

Advocates and bureaucrats aren't easily hybridized. Advocates, if they are genuine, are focused on a single, defined set of issues. Under normal circumstances, advocates work on behalf of constituents, and they couldn't care less about competing priorities. Bureaucrats usually move with caution, considering institutional interests and practicing the art of the possible.

What should one expect from a "regulator/advocate"?

Expect a sense of urgency. Expect impatience. Indeed, if you know where you are going, why not move fast?

Consider this recent action on the part of the agency:

On March 4, FDA announced approval of the Bristol-Myers Squibb drug Opdivo (nivolumab) in metastatic squamous non-small cell lung cancer. The

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An interview with Rick Pazdur and his wife, Mary. The interview was conducted by Ellen Stovall, senior health policy advisor of the National Coalition for Cancer Survivorship. The full video is available on The Cancer Letter website.

action was almost certainly unprecedented, because the agency received the data and sprung into action—read this carefully—*before the results were unblinded to the sponsor.*

"With regard to the impetus for this rapid action, we began working immediately on this review and submission strategy after being informed of the survival results. This was prior to BMS having been informed of the results since they were still blinded," Pazdur said matter-of-factly to The Cancer Letter (The Cancer Letter, June 2). "Patients and physicians need to be informed about these findings and this was the impetus for the rapid inclusion of the survival data in product labeling."

Some changes are hard to miss, and people who know the Pazdurs pretty much uniformly note the change of tone in Rick's remarks and a new sense of urgency in his actions.

"It's a huge loss, and I think he has been using this experience—I don't know whether consciously or subconsciously—to impact major changes in such a short period of time as to how we are redefining drug development and drug approval. It's very outside the box," said Patricia LoRusso, associate director of innovative medicine at Yale Cancer Center and one of Rick's former trainees.

"Rick—as many caregivers of cancer patients—realizes the urgency. He may speak as an activist, but I think he also thinks as a brilliant drug regulator. He may come across as an activist, but I think his brilliance always made him an activist. It could look like he is an activist, but when you know Rick, you know a very outside-the-box thinker," said LoRusso.

"He is the kind of person who can solve the problems."

FOCR's Sigal, too, sees the new urgency. "I think he has changed. I don't think that he is prepared to put junk products on the market, to loosen standards," said Sigal. "I think the toxicity, and the urgency, and the quality of life issues change you when you see them first-hand."

Same goes for NCCS's Stovall: "Mary's diagnosis heightened Rick's interest in the way cancer patients are treated in our healthcare system and that no matter who you know or how much you know, the limitations of the science are the harsh realities he an others have to face when a loved one has cancer," she said to The Cancer Letter.

"Both Rick and Mary expressed to me that they didn't want or expect any special treatment simply

because of his position with the FDA. I do think because of Mary's professional role as an oncology nurse at NIH, and Rick's distinctive knowledge of emerging therapies, that their mutual respect for the science gave them a lens through which to view the realities of what would be in store.

"Did these realities change Rick and alter his views of regulatory processes? I don't believe so. I do believe that his sense of urgency about getting promising drugs through the regulatory system expediently, but responsibly, was top of mind for him throughout his career and remains his steadfast goal.

"I do believe that Mary's diagnosis widened his awareness of what families experience when treatments become futile, and how frustrating it is that we can do so little for someone with advanced cancer.

"I feel certain that his awareness will serve to strengthen his resolve to continue to reform the FDA to best serve the interests of all of us who rely on that agency to be a standard-bearer for excellence in expediting well designed drug development plans and approval of effective new oncology therapies."

Where Detroit Is

Rick and Mary met in June 1979, on the first day of his oncology fellowship at Rush Presbyterian Hospital in Chicago, where Mary Patricia Bagby was a nurse.

Both were as Chicago as it gets. Rick comes from a Polish family in the grimy, industrial Calumet City, Mary from a large Catholic family in Tinley Park, also south of the city.

"If she had my mother, she would be chief of neurosurgery at Mass General," said Rick recently. But nursing was the traditional occupation for women in the Bagby family. Mary's mother, Shirley Bagby, was a nurse, as are her three sisters. "She won academic awards," said Pazdur. "She could have done anything she wanted to, and she chose nursing, because she wanted to help people."

"It's hard for me to talk about her without crying," said Arthur Rossof, who worked with Mary and Rick when he was a junior attending physician at Rush. "Mary was always a tranquil, anchoring voice, she was always in control, she always had nice things to say about people, projecting the attitude of we'll get through this, and we will get it right, and everybody will be taken care of."

Mary and Rick started dating two years after they met, and were married in 1982, as Rick was preparing to move to Wayne State University.

"You don't even know where Detroit is," said Mary at the time.

"Yeah, it's someplace east of South Bend," Rick conceded. Their honeymoon was in Detroit.

"When Mary smiled, she always had that sparkle in her eyes, it was just so special," said LoRusso, who was trained by Pazdur at Wayne State. "She was such a basically positive person. She had such a gentle soul."

Six years later, in 1988, the Pazdurs moved to MD Anderson Cancer Center, and in the mid-nineties, in interactions with FDA over clinical trials of the drug UFT, an oral version of 5-fluorouracil, Rick realized that the agency might be an interesting place to work.

Roy Herbst got to work with Mary when he was a junior attending physician and she ran the practice of Waun Ki Hong, chair of the Department of Thoracic/Head & Neck Medical Oncology at MD Anderson.

"Mary was sort of the dean of our nurse practitioners there," said Herbst, now chief of medical oncology at Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven.

Rick applied for the job to head the oncology division at the FDA Center for Drug Evaluation and Research, but didn't get hired on the first try. The job went to Robert DeLap instead. In 1999, the job opened again after DeLap moved to regulation of over-the-counter drugs.

"I don't want to get Rick mad, but I remember when Rick left, we all missed him at MD Anderson, but we missed Mary at Thoracic/Head & Neck more," said Herbst.

"And here at Yale, I have just recently recruited a fellow from NCI who had trained under her," Herbst said. "I knew that if he worked with Mary, he must have had some good training."

Politics of cancer wasn't Mary's world, but after the couple's moved to Bethesda and she took a job at the Clinical Center, she relied on her God-given intolerance of nonsense to become a clear-headed observer and advisor to Rick.

"She was the sounding board," Rick said. "How could she not be? You discuss things. During the hard times she was there."

Paul Kluetz, who is now the acting deputy director at the FDA Office of Hematology and Oncology Products, met Mary in the beginning of his fellowship at NCI in 2008.

"I was eager to learn what it takes to become a great oncologist, how to confront the challenge of providing empathy and compassion while taking care not to allow the inevitable losses to hit too hard, derailing my mission to continue to help the next patient. This is

a continuous balancing act," Kluetz said.

"At the time, Mary worked with Bill Dahut's group [the Prostate Cancer Clinical Research Section], and I had gravitated toward his busy clinic at the NCIs Clinical Center. As a new fellow, I remember getting to know Mary—and being struck by her combination of efficiency and great humanity, her compassion and strength.

"She frequently saw more patients than any other nurse in the clinic. The patients and their families loved her. She cut to the chase, she had a great sense of humor and an infectious laugh—and she cared. Deeply."

FDA, 16 Years Ago

In 1999, FDA's cancer portfolio was splintered, with small-molecule drugs going to one division and biologics to another.

The word in the street was that to get your drug approved you needed two randomized trials showing an improvement in survival.

There was a de facto shortcut—accelerated approval, which allowed the use of surrogate endpoints, primarily tumor shrinkage. The best way to get an accelerated approval was to conduct a large, usually single-arm, phase II study, enrolling 100 patients or more.

Many times, these trials demonstrated small, marginal response rates that raised questions about their utility. But the advantage of accelerated approval was a fast route to approval with a small data set that didn't require a large randomized trial of hundred of patients.

In what could be described as the first phase of his career at the agency, Pazdur combined an emphasis on randomization with the search for endpoints other than survival. This met with protests on the part of groups that opposed randomization, some for ideological reasons.

The Wall Street Journal's editorial pages singled out Pazdur as FDA's "Dr. No," building on a theme of opposition to the efficacy standard and the IND requirements.

Editorial pages included stories titled "Pazdur's Revenge," "Pazdur's Cancer Rules," and "Pazdur is What the Doctor Ordered." The newspaper's editorialists described the oncologist as a "hyper-cautious" man of "anti-industry views" who insists on costly and unethical placebo-controlled trials, and is determined to use mind-numbing minutiae to drive American's cancer sufferers into the grave by denying them access to life-saving drugs.

Decisions attributed to Pazdur triggered demonstrations, vicious posts on the Web, and lawsuits. All of this made friends worry about the Pazdurs' physical safety (The Cancer Letter, Aug. 5, 2005).

Yet, even in situations where others accepted protection, the Pazdurs did not. Threats notwithstanding, they continued with their routines, which included buying cool stuff and useless tchotchkes at estate sales, taking care of their garden and playing with their tiny, snow-white Maltese dogs.

One of them, a rescue Maltese named Moshe, loved Mary, but, akin to The Wall Street Journal editorialists, took every opportunity bite Rick.

Tag Team Storytelling

Yale's Herbst says that Pazdur's achievements at FDA include building a strong team of medical reviewers. This required making regulatory science into an exciting career path for young oncologists.

Over the past five years, Pazdur's office hired many former NCI fellows, all of them unofficially pre-screened by Mary.

"I remember someone at NCI saying to me, 'Don't you know who Mary's husband is? It's Rick Pazdur!'" Kluetz recalled. "Not being familiar with the FDA at the time, I didn't really know who the guy was.

"As I began to work closely with Rick at FDA, my relationship with Mary changed a bit. I got the opportunity to get to know her outside the clinic as a friend. It has really been a pleasure to get to see how Mary and Rick were as a couple, the way they looked at each other knowingly and smiling during conversation, how they reminisced about great trips and adventures they had taken. They were complementary, and they were tag team storytellers.

"Mary would set the scene, Rick would flesh out the characters and play out the events, taking it to the extremes of appropriateness and beyond, and the story would be punctuated by a Mary Pazdur laugh, usually a half-hearted reprimand—'Oh Rick!'—and a knowing smile."

"Integration"

Pazdur's emphasis on randomization has made it possible to change the endpoints for some diseases from survival to slowing down disease progression, and with the industry mostly pleased, the protests haven't been heard in recent years.

And as science changed and drugs became more precise, Pazdur's office found a methodology to approve them quickly.

Because of the new crop of drugs over the past few years have far more impressive response rates, single arm trials have come back into vogue. "The drugs just got better," Pazdur said to The Cancer Letter. "We are no longer taking about response rates of 10-15 percent,

but rate exceeding 50-60 percent."

So far this year, the hematology and oncology office approved 15 new molecular entities—and almost 40 percent of breakthrough therapies are in oncology.

At the recent FOCR meeting, Pazdur said he believes that FDA's oncology portfolio needs to be further consolidated.

"Our orientation toward a specific problem is a reflection of legislation—much of that emanated from the 1960s," he said. "I ask each one of you, have you changed since 1962? And I think if you haven't, there's something fundamentally wrong with you.

"I'll use a phrase that my wife uses. And I'll answer it as she would answer this question. Who likes change? A baby with a wet diaper.

"The purpose of the FDA is ultimately to serve the American public and get these drugs out in the most efficient means as possible… People need to have the structure and the foresight to see that this is coming. Whether it's in my lifetime or not, it will be done because it's the right thing to do."

Sigal agrees. FDA needs to integrate its cancer portfolio, she said to The Cancer Letter.

"You don't go to a doctor for CDRH or CDER. You go to a doctor for your disease. When you are regulating this disease, the integration of disciplines is extremely important," she said. "I have never gone against FDA—ever. I have always worked with them. And I have always been genuine partners with them. But this time I am willing to make a lot of noise."

Exactly a week after Pazdur spoke at the FOCR event, Mary succumbed to her disease.

The funeral service at St. Jane de Chantal Catholic Church on Dec. 1, a few blocks from the couple's house, was followed by a gathering in the church basement. The food was Middle Eastern, prepared by the Syrian immigrant who cooks at the Montgomery County Hospice.

Mary hired her to make sure that the last arrangements she will ever make would help someone establish a new life in a new country.

She will miss the next act in Rick's career, the phase that her illness inspired.

In addition to Rick, she is survived by father David Bagby and siblings Michael Bagby, Larry Bagby, Debbie Brower, Patty Ortiz, Peter Bagby, Martha Baggetto and Joseph Bagby.

In lieu of flowers, memorial donations can be made to Marcella Niehoff School of Nursing, Loyola University of Chicago, Health Sciences Campus, 2160 S. First Ave., Building 120, Suite 300, Maywood, IL 60153—or to the Christ Child Sodality of St. Jane's Church.

Rick's Search for Meaning

(Continued from page 1)

"What we're seeing now is not a patient voice but a patient cry—wanting to have their position heard," said Pazdur, speaking at a Washington conference sponsored by Friends of Cancer Research.

At the time, Pazdur's wife Mary was at the Montgomery County Hospice. She died of ovarian cancer a week later.

Pazdur spoke with Ellen Sigal, the group's chair and founder. Their conversation follows:

ELLEN SIGAL: *I think everybody knows that cancer is personal and it touches all of us. And it certainly touched you in a very profound way with Mary's illness. Talk a little bit about what that has taught you; what you need to do—how is it different? Because we've all seen people suffer every day, but when it's a spouse, it is different.*

RICHARD PAZDUR: About three years ago, my wife was diagnosed with ovarian cancer. And during this three-year period of time, we've seen the entire spectrum of medical care, and, unfortunately, at this point she is undergoing hospice care and has come to the decision of what she wants to do with the remaining months and weeks.

It's a very difficult time.

This three-year period of time has given us the opportunity for observation of the healthcare system from the other side of the stethoscope. You see the worst of the system; you're not immune just because you're a doctor or a member of a doctor's family. You're not immune from the mistakes that happen—people forget to order X-rays, people give you the wrong laboratory results. These things just happen, and people have to be accepting.

When Mary received the original diagnosis, we wanted to take a very aggressive approach very early on. But we were very realistic about when was the time to call it quits. Unfortunately, many people are unwilling or cannot accept the issue of when it is time to stop therapy and to accept hospice care.

Fortunately, my wife, Mary, had a 35-plus-year history of working in the in oncology and understood the disease process.

She had taken care of similar patients as herself. She had a very good understanding and she has mentioned this throughout our conversations during this period that perhaps these prior experiences with other oncology patients were rehearsals for what she is going through now.

But how has it influenced me? That's a very difficult question, because you're not the same person that you were yesterday. You won't be the same person in a week. We're constantly evolving and there are numerous things that impact us.

Not only our personal life and our professional life change our perspectives, but the drugs that come out during this three-year period of time have really transformed what we're doing.

From a personal perspective, we underestimate toxicity. Doctors spend only a short time with patients in exam rooms. They don't really see the entire spectrum of toxicities, how long they last, how they impact patients' lives.

And that was one of the reasons we initiated a regulatory interest in incorporating PRO CTCA into describing toxicities. How can we better incorporate the patients' perspectives in describing toxicities should be a goal.

During this three-year period I had issues confronting expanded access. Even in my position, it is not easy to get an unapproved drug for a patient. I've had two former NCI directors that couldn't figure out how to maneuver or navigate through expanded access process.

As an agency, we have to develop a better system—all the parts are there—but they are not coordinated. I'm not saying that every drug company needs to give patients drugs that are unapproved. We have to have a process that works better.

In addition, we have to have a clinical trials system also that makes it easier to enroll patients who may not fit very exacting eligibility criteria—performance status, previous malignancies, HIV status. We probably should take a much harder look at what a real world experience is with a drug. That's the way it's going to be used.

ES: *Has Mary's illness given you more of an urgency?*

RP: Yes. Time is not equal. People have to understand in drug development, that when a drug is undergoing phase I studies, people don't know the activity of the drug, and there might not be that urgency. However, when one sees activity in a very refractory disease setting, and the patient realizes that this drug is an important drug they want that drug.

I've stated to ASCO that they need to have an announcement regarding plans for expanded access at their annual meeting when a novel drug that has activity in a refractory disease is presented. Patients want that drug—there has to be some acknowledgment during that presentation about what will be the expanded access of that unapproved drug.

Time is not equal in drug development, and most patients understand that, and most practicing physicians understand that.

There is a need to expedite clinical trials. Patients want expansion cohorts in phase I studies. They want early access to drugs. We don't necessarily need to be married to a survival endpoint in a phase III trial. The basic purpose of the FDA is to get safe and effective drugs out to patients. It's not the protection of the p-value or a statistical principle.

ES: *Which is incredibly important. When you came to FDA, we worked with FDA about 10 years ago to talk about a move of biologics to CBER from CDER. That was extraordinarily difficult. It was the consensus of the community that this needed to happen.*

Most recently, we wrote an op-ed in The Hill about further consolidation of disease. We think that we have to go to the next step. We have to look at how we are not training CDRH, CBER or CDER—we are treating patients with disease. And the further integration, in a more meaningful way, we think is going to be essential.

We suggested three pilots, one of which in cancer, which we think is the most ready, but also in cardiovascular or perhaps in Alzheimer's or the neurodegenerative diseases. We have this in legislation, if it ever comes out. I know that there are varying views. It may be difficult, but perhaps you can talk a little about it?

RP: These are my own personal opinions; not FDA's. I think society has changed. Our current regulatory orientation is a reflection of legislation that emanated from the 1960s. I ask each one of you, have you changed since 1962? And I think if you haven't, there's something fundamentally wrong with you.

Society has changed since 1962, and its expectations of the agency have also changed. However, the existing structure remains similar to that of what it was 50-60 years ago.

I like to remind people that the FDA has two missions—the protection of the American public and the promotion of the health of the American public. And many times we forget the second, very important mission is that of promotion.

Society has changed. People want FDA to be much more active and engaged in drug development—not just a regulatory body, but an organization that's involved in the development of drugs. It's a different perspective than 50 or 60 years ago, and hence the structure needs to change to reflect society's changing expectation of the FDA.

A patient doesn't go to a doctor to get a drug,

device or to get a biologic therapy. They go to a doctor to get a treatment for a specific disease.

When we reorganized the oncology divisions into specific diseases, we witnessed a transformation in the staff. They become much more involved with the community and investigators.

Initially there was a great deal of consternation among the staff when I proposed the reorganization. People said, "Oh, we can't do this, this is the worst thing. I want to be a generalist. I want to see all diseases."

Well, those days are gone. In oncology you need to have expertise in a specific disease.

The number of drugs that we're approving is escalating. If the moon and the stars align, we may approve up to 15 new molecular entities this calendar year in oncology.

The field is dramatically changing. You have to be flexible. In order to do that, you need people that have expertise in the disease, not just in drug regulation. What's important is not just looking at the trial's statistical design and making a decision, but understanding what's going on in the field and the importance of the drug to patients.

We have excellent statisticians who help us tremendously. We don't need to duplicate their work. We have to bring a different perspective. And part of that perspective is not only the application but working with people before that application arrives. That's part of the Breakthrough Therapy designation

ES: *So the integration of experts, whether they're from CDRH, CBER—really would make a huge difference, because they all clearly have an enormous expertise in their field, but the integration certainly would help as we've seen in monoclonal antibodies. Do you think change can happen from within? It's always been our core belief that this is very difficult and it has to be driven by, frankly, the stakeholders, including patients. Do you think this is possible?*

RP: I don't know. I'll quote my wife: "Who likes change? A baby with a wet diaper."

People have entrenched interests. Many people inherently do not like change. With the initial change in bringing the biologic products into CDER a decade ago, there was a difficulty and tension within the agency. Even with a small change within our office in forming disease-specific teams there was resistance.

The purpose of the FDA is ultimately to serve the American public and get these drugs out in the most efficient means as possible. We're not here to serve our employees. There may be some "unhappiness" that some employees would be displaced or have to be moved around. My answer to that would be: Get over it.

It's really something that needs to be done. People need to have the foresight to see that change is coming. Whether it's in my lifetime or not, it will happen because it's the right thing to do.

ES: *I would say that we would agree with you, at least many of us. So this conference has changed a lot of behavior. We do it because of you, and because of NCI and because of all the stakeholders together. I don't think anyone would have ever thought that we would come through, but what people don't know is that much of the innovation has come from questions that have been posed to us.*

Breakthrough was your first question to us. It wasn't just what should we do. And I can tell you that was not easy, there wasn't a huge bed of consensus, and it was hard to imagine what the outcome would be and certainly many other things.

Do you have other questions for us? We think that if everybody is working together, we can change the climate. Do you have any other instructions for us?

RP: You alluded to my wife's experience during this period of time, and that experience underscores to me the need for more active patient involvement in the process.

I have had time to reflect on patient advocacy in general. I have morphed from the "regulator" to the unique position of a "regulator/advocate."

As I look at our initiative of the "patient voice" at the FDA, and I wonder if we should focus on bigger questions. When we do incorporate patients into discussion, what should be the purpose of the patient on a panel or meeting? Patients have different perspectives. Someone who has an adjuvant therapy experience—a chance of having a recurrence—may have a much different perspective than someone who is battling advanced disease and has few therapeutic options.

I really would encourage the advocacy community to focus on big questions—such as whether we should use survival or time to progression. We need to focus big picture questions.

We want clinical trials that work for us. Expanding the eligibility criteria is needed. We need an informed consent process that works for us. Patients currently receive all these pages of legalese that lead to confusion. When my wife went through informed consent, I started reading it and threw it on the coffee table and said, "Mary, do what you want—you have to trust your doctor—but this form isn't going to help you make any decisions. It's just going to confuse things."

Throughout these 15 years or 16 years that I've

been at the agency, we've had numerous discussions about what endpoints should be. These discussions are constantly evolving. When someone talks about the patient voice, there's not a single patient voice, but a chorus of voices.

What we're seeing now is not a patient voice but a patient cry—wanting to have their position heard.

The position of a patient should be defined by the patient—not by somebody else. Certainly not by the FDA, and not by the pharmaceutical industry nor the clinical trial enterprise—a multi-billion dollar enterprise. Rather than the patients being asked to come and comment about a predefined issue, patients need to direct the show.

So the question I have for the patients is, "what do you want?" You need to run the show—not the FDA, not the NCI, and not the pharmaceutical companies. Ultimately, the clinical trials are about you.

NCI Director's Report

Doug Lowy Addresses Dec. 1 NCAB-BSA Joint Meeting

(Continued from page 1)

The number of R01 awards fell short of pre-sequestration levels, but there has been a substantial increase in R21 applications—from 225 in 2012 to about 355 in 2015.

"What I would like you to see is that when sequestration happened there was a major reduction in the budget for the NCI; a reduction of $275 million compared to FY 12," Lowy said at the meeting Dec. 1.

"There was a much more modest reduction in the competing RPGs from FY 12 to FY 13. Then in FY 14 and FY 15, we had added about $50 million in each of these two years; these are additive for the RPG pool.

"This is with there having been about a $140 million increase in FY 14 and just a $21 million increase in the NCI budget. So just to put into context what has happened with the RPG pool, in the context of the overall budget situation.

"We are still on a continuing resolution which makes it harder for us to function at full capacity."

The text of Lowy's remarks to the NCAB and BSA follows:

I would like to express my welcome for everyone and also especially for the new members of the NCAB and BSA. I want to bring you up to date on a number of areas since we met back in June.

I want to talk about the RPG success rates from FY 15; the new Research Specialist Award; the new cryo-EM user facility at the Frederick National Laboratory for Cancer Research; the cancer health disparities workshop held a couple of weeks ago; the new pilot project with the Department of Energy; and then the MATCH trial update, which Jim will discuss.

Last week, we put up the data from FY 15 for the RPG success rates, etc., and the detailed report is available here at the NCI website, either through this URL or you can go directly to the main part of the website and access it through there.

I have repeated one of the tables, because it gives you some information about has happened the last four years with success rates for the different kinds of applications. The FY 12 is on the right and FY 15 is on the left. I highlighted in red what has happened with the R01s, and if you look at the total number of R01s, we had about 660 that were given in 2012 and about 635 in 2015. The number from 2015 is larger than it was in 2013 or 2014—2013 is when sequestration occurred and we had a 5 percent decrease in NCI budget and the NIH budget overall.

Here I have highlighted the R21 applications and the success rate for the R21 applications has been somewhat less than that for the R01 application, which has remained at 14 or 15 percent. The success rate has gone actually up from 10 percent in FY 12 to 12 percent in the last couple of years. We have also maintained the increase—there was a substantial increase that I discussed a year ago in 2012, we only funded about 225 R21 applications. This number went up by 125, to 355 in 2014, with a similar number in 2015.

As we have discussed before, the Outstanding Investigator Award were first made in FY 15, so this is on top of the R01 and R21 awards that were made this year.

On this slide, I have depicted for you the competing RPGs, this is the dollar amount on the top line. This on the second line is the change from the previous year in millions of dollars. Then on the third line is the total NCI budget for those years and then the change from the previous year. Here FY 12 is on the left and FY 15 is on the right.

What I would like you to see is that when sequestration happened there was a major reduction in the budget for the NCI; a reduction of $275 million compared to FY 12. There was a much more modest reduction in the competing RPGs from FY 12 to FY 13. Then in FY 14 and FY 15, we had added about $50 million in each of these two years; these are additive

for the RPG pool. This is with there having been about a $140 million increase in FY 14 and just a $21 million increase in the NCI budget. So just to put into context what has happened with the RPG pool, in the context of the overall budget situation.

As I mentioned, the addition of the Outstanding Investigator Award will continue to put pressure on R01 and R21 awards, but we hope we can maintain those numbers, and certainly if we get the president's budget and you will hear from MK Holohan [Quattrocchi, acting director of the NCI Office of Government and Congressional Relations] after our presentation with the legislative update, you will hear about the status of the FY 16 budget. We are still on a continuing resolution which makes it harder for us to function at full capacity.

So in the last few weeks we had approval for the R50 Research Specialist Award that Dinah Singer [director of the NCI Division of Cancer Biology] has discussed previously. The applications are due Feb. 9. The purpose or intent is to support a new career path with stable salary support for accomplished scientists who want to continue to do research but who do not want to be a PI. This is a five-year award and it is potentially renewable. It would support that portion of salary dedicated to NCI-funded cancer research by the PI. It wouldn't cover research expenses, but could include travel funds of up to $5,000 per year.

The application requires a letter from the sponsoring principal investigator—but grantees, that is, the research specialist, would have independence to move to another lab or institution, but with prior approval from NCI.

This is to try to give some prominent stability to a very important part of our research enterprise, the research specialist. Just as we tried to give prominence to the outstanding investigators with the Outstanding Investigator Award.

New Cryo-EM at Frederick

Now I would like to turn our attention to establishing a cryo-electron microscopy user facility at the Frederick National Laboratory for Cancer Research.

The goal here is to provide extramural research community access to high-quality cryo-EM so that by developing high-quality images, it will be possible to determine structures of macro molecules of importance in cancer research. On September 30th, the Frederick National Laboratory advisory committee, which is headed by [BSA member] Joe Gray [director of the Center for Spatial Systems Biomedicine at Oregon Health and Science University], who is here today, discussed a presentation by Dr. [Sriram] Subramaniam [head of the Biophysics Section of the NCI Laboratory of Cell Biology].

This was his third presentation, instead of striking out, the third time was the charm, and the advisory committee recommended, essentially unanimously, to go forward with this program. And so we have instituted it.

There will be a steering committee for user facility and it will be composed of members of the advisory committee, the cryo-EM community, and the structural biology community. And Sriram will be the facility director at least for now.

We are proposing there be a modest user fee, far less than the cost of recovery, but this was discussed by the advisory committee and seems to make sense so there was some commitment on the part of the laboratory that was using it.

The Titan Krios [electron microscope] that was going to be the workhorse for this user facility arrived at the end of September, and we are leveraging the investment by the Center for Cancer Research, intramural program, in cryo-EM technology which made it more cost effective for us to set up the user facility.

The purpose is the potential for determining high resolution without three dimensional crystals, structural analysis of dynamic protein assemblies, and progressively higher resolution, as you'll see on the next slide.

You can map conformational states of integral membrane proteins, localization of drug binding sites, and a relatively high degree of automation in data collection and processing. This next slide shows you how the resolution has increased substantially over the last dozen years or so, from about 9-angstrom resolution in the early 2000s, to 2.2-angstrom resolution this year.

This has led to a lot of high profile papers that use cryo-electron microscopy, with this nice pun in Nature saying the revolution will not be crystalized.

Cancer Health Disparities

I would like to talk now about the NCI workshop on cancer health disparities. This is just one part of our effort to develop research priorities for NCI in cancer health disparities.

The workshop was held three weeks ago. Lisa Richardson [director of the CDC Division of Cancer Prevention and Control], Edith Mitchell [director of

the Center to Eliminate Cancer Disparities at Thomas Jefferson University], Sandy Markowitz [head of the Cancer Genetics Program at the Case Western Comprehensive Cancer Center], and L. Michelle Bennett [director of the NCI Center for Research Strategy] were co-chairs.

It focused on a few cancers—all which have health disparities, not just in terms of incidence, but importantly in terms of mortality rate: breast, prostate, colorectal, liver, multiple myeloma. There are several different under-represented minorities that have increased risk of developing liver cancer as well as dying from it. And liver cancer is the cancer in the United States whose incidence and mortality are increasing faster than that of any other.

So the overall questions we were asking was what accounts for the elevated risk in these high risk populations—biology, lifestyle, access, and utilization—and what can be done to mitigate the risk in the short-term, intermediate-term, and long-term.

There were two overarching research areas that were discussed. This is just one of many proposals that were made during the meeting. I want people to understand that we haven't really decided what is going to happen. We're going to have an internal meeting next week and we'll solicit more information from others before deciding what our research priorities are actually going to be.

One possibility was to develop and study a cohort focused on minority individuals who develop cancer at an unusually early age, it could address roles of genomics, environment, biology, screening, treatment, and other causal factors or associated factors. Another area was financial toxicity: understanding it, and understanding how to try to overcome it.

My own feeling is that the area of financial toxicity is a very important one, but although there is a certain amount of research still to be done in it, a lot of it is really deals with the area of implementation, and I hope there will be other entities that will try to champion overcoming this area.

I now would like to turn to one example, which is colorectal cancer—one of the areas that was discussed—and just to reiterate for you there is this increased incidence and mortality that's gone on for many years among African Americans.

Some of the research questions that were proposed were what are the best algorithms to follow for screening and for follow-up? What would be effective, acceptable, feasible and scalable?

Barry Kramer [director of the NCI Division of Cancer Prevention] has often said the best colorectal cancer screening test is one you are willing to take.

But we want to see if we can try to put really some specificity to this, and one of the areas that we're thinking of trying to work with other groups outside of the NIH is with PCORI, the Patient-Centered Outcome Research Institute, to work with them with joint funding to look at issues such as screening for this or possibly screening with breast cancer or other areas.

We met with Joe Selby last month, who is the head of PCORI, and we're planning to meet again with him and several members of his group next month to try to go forward and be more precise what we might try to work on together.

And then effectiveness of prevention, chemoprevention and lifestyle factors. I mentioned at the virtual meeting of the NCAB back in September, the U.S. Preventative Services Task Force made a draft recommendation for the first time for use of aspirin to reduce the incidence and mortality from colorectal cancer. The final recommendations for colorectal cancer reduction are expected in 2016, and we suspect they're likely for all populations eligible for aspirin for reducing risk of cardiovascular disease within a certain age range. Therefore, the recommendation for reducing colorectal cancer risk will be tied to the recommendation for reducing the risk of cardiovascular disease.

During the meeting for health disparities, I looked up the uptake has been among African Americans for the use of aspirin for reducing cardiovascular disease, and this is a recommendation that was made more than ten years ago. Aspirin uptake for reducing risk actually is substantially lower in several different reports for African Americans. Therefore, two weeks ago I spoke with Gary Gibbons, director of NHLBI, and we are going to explore the possibility of a joint project to promote the use of aspirin to prevent cardiovascular and colorectal cancer. Obviously this would be for minority populations as well as for other populations.

Michelle Bennett, Worta McCaskill-Stevens [chief of the NCI Community Oncology and Prevention Trials Research Group] and Sanya Springfield [director of the NCI Center to Reduce Cancer Health Disparities] did a Cancer Currents blog at the beginning of this month and they discussed efforts in biology clinical trials and training a more diverse work force. And we're asking people in the community to join in conversation to share thoughts, ideas and recommendations.

Predictive Models in Precision Medicine

The last subject is the work that we're planning to do with the Department of Energy to try to use their high exoscale computing, and Warren Kibbe [director of the NCI Center for Biomedical Informatics and Information Technology] here at the NCI has worked closely with Dimitri Kusnezov [chief scientist and senior advisor to the secretary] at the Department of Energy to forge this pilot program. Basically, the Department of Energy has really a lot of expertise with computing, data analysis and experiment-driven co-design of extreme scale simulation—and needless to say we have a lot of interest in precision oncology research and clinical applications.

So we're trying to put these two together to have advance computing solutions for cancer. One of the pilot projects that we're proposing to do is to use predictive models for pre-clinical screening with the goal of improving those predictions. This is part of the oncology portion of the Precision Medicine Initiative. The projected timeline for doing this is shown here.

The overall goal is to try to see: Can we come up with highly predictive models of what the biology of tumors will be and what the response will be to various kinds of treatment?

I'm now going to turn the microphone over to Jim Doroshow [director of the NCI Division of Cancer Treatment and Diagnosis] who will bring you up to date on what has been happening with the MATCH trial, which is also foundational for the oncology part of the Precision Medicine Initiative.

DOROSHOW: Thanks, Doug. I will try to be brief because we have a lot other things that we want to hear about.

But first let me remind you that the match study was initiated about the middle of August. Under leadership of the ECOG-ACRIN cooperative group, and also a group from the NCI, Barbara Conley, Alice Chen, and Jeff Abrams and others worked tirelessly to get that study off the ground.

So I'm delighted to report to you that in approximately eight or nine weeks, the trial accrued over 500 patients. At one point 70 patients per week—the fastest treatment trial accrual ever in the history of NCI-supported clinical trials, which is really quite remarkable since significant portion of the accrual came from the community. With physicians over the country, part of our NCORP group submitting samples to one of four different laboratories that did sequencing, and one base laboratory that evaluated the materials that were sent. This is really a national effort at both university medical center and community clinical practice milieu.

Because of that fast accrual, based on what was pre-specified in the study, that the study is now on a pause. It was specified in the protocol that once we got to 500 patients—which we thought would be toward the end of the first year, not after two months—there would be a pause to look at the accrual, the characteristics of the patient population.

Again, I think some of you know and maybe others don't—the way the trial was written, about 25 percent screenings are reserved for rare cancers, so we need to look at who has been accrued, what the distribution of diseases might be, what the distribution of patient characteristics are.

And this is an opportune time because we expect that by the time the study is reopened for accrual, hopefully in January, we will have the time working with central IRB which has been working just incredibly hard to try to open an additional seven or ten additional drug treatment arms that will broaden range of drugs available to patients from 10 to between 10 to 17 or 20 or 21 which will also be useful for patients.

It's a remarkable experience. We also learned the limits of our capacity. The other reason for thinking this pause is a good idea is that we're in the process of trying to open and find two additional laboratories to provide help in the sequencing effort, because we expect that the accrual will be very rapid once we reopen.

So I think that this is a remarkable activity that have is involved, for those who don't know, literally hundreds of individuals—scientists, clinical trialists, statisticians—to try to make this activity happen. So we're very proud of the way the community has responded.

JACKS: Thanks, Doug, and thanks, Jim. So we have time for questions.

CHERYL WALKER [BSA member and director of the Institute of Biosciences and Technology at Texas A&M Health Science Center]: So I think it would be helpful to have, along with the success rates for RPGs, some sense of what's happening to the funding levels. I think it would be nice to, for example, to see for grants that have requested modular budgets, what percent has actually has been awarded. And then for larger grants, how that has gone, and to be able to look at that over time. I think would be useful if we can have that information as well.

LOWY: Sure. I presented some that have information a year ago here at the joint board meeting.

We can certainly update it. One of the things that we did as a result of that meeting and follow up was to essentially take the automatic 17 percent cut that we were making in the modular grants and make it only an 8.5 percent cut.

We would like to eliminate that 8.5 percent cut but I will tell you that I am reluctant to do that at this point, because if we were to do that it would add another $10 million essentially to the cost of the modular grants. I would rather at this point try to take that money and use it for more grants rather than for doing that. If we got substantial increase, especially in a sustained rate, for the NCI appropriation, that would be one of the first things to go, if you will.

KEVIN SHANNON [BSA member and American Cancer Society Research Professor at the University of California, San Francisco]: Jim and Doug, I wanted you to maybe fill in a few more details about the pre-clinical effort. It seems to me the three-year timeline to actually figure out if things are working and are predictive seems a little unrealistic.

What's the sort of—obviously cell lines are cell lines—but for the PDXs, is it going to be a pilot where they treat the PDXs with the same drugs the patients got to see? How do you actually know if something is predictive? We used to fight about this in the mouse models consortium all the time, and I didn't see anything in there that made me confident that in a two-to-three-year window that you can actually answer the predictive question with any sort of precision.

DOROSHOW: I have to agree with you, it's a very aggressive timeline. What we are in fact doing a fairly large pre-clinical, clinical trial, mimicking the IMPACT trial that is a randomized trial of matching drugs to mutations in pre-clinical models. So we will have a considerable amount of therapeutic data across a large enough number of models, and a large enough number of animals, that we'll have all have been sequenced and have substantial amount of information over the course of at least the first year and a half, to be able to provide them with DOE computer folks with very interesting data.

Is it going to be done in three years? It's probably not going to be done in three years.

LOWY: Kevin, I want to make it clear, that what I was talking about with the Department of Energy is a pilot program, and not expecting to solve everything by FY 18.

SHANNON: Can you comment on just the clono-heterogeneity issue and how that might be dealt with in this effort? Neither PDXs, nor cell lines recapitulate that. As near as I can tell, a very large proportion of cancer drug resistance and relapse is due to inherent genetic instability and heterogeneity.

DOROSHOW: one of the very strong outputs of presentation made to the Frederick committee a couple of months ago about the models, was a really very insightful suggestion, which we're going to follow-up on. To actually work with several of the sites that do fast autopsies. To actually obtain from an individual patient a series of different biopsies at autopsy, so that we start to have models that in an individual patient might reflect some of the heterogeneity that you're talking about.

KEVIN WHITE [BSA member and director of the Institute for Genomics and Systems Biology at The University of Chicago]**:** The accrual in the MATCH trial is spectacular. And what it brought to mind was the challenge of getting the sequencing data, the anonymized clinical records data, the outcomes data from those patients out the general community, you may have to take steps to speed up that process. Could you talk about what steps you may take and what the timeline might be until the general scientist out there can plow through the data?

DOROSHOW: The last clause I don't know the answer to, because it depends how fast we complete the trial.

The first part of your question I think is a critical one, we spent time trying to model how much in terms of additional resources need to go out to the sites that are doing the sequencing, to be able to bring them up to speed to deal with the volume.

So basically the numbers are pretty clear. If we actually continue to get 70 accruals per week we'd be done with trial in a year. So the resources have to be brought forward from year two, year three to be able to provide what's necessary for the sites that are doing sequencing, and also the tissue preparation to give them the resources to handle that volume. I'm not sure that the volume will continue exactly at that level but we've made substantial contingency plans and will provide additional resources to those sites to be able to handle the load.

BARBARA CONLEY [associate director of the Cancer Diagnosis Program in the NCI Division of Cancer Treatment and Diagnosis]**:** I think this is a stellar discussion but it's my understanding that with any trials we share the data after publication? So as each arm would finish that would be a publication and data shared; is that still correct?

DOROSHOW: This is an umbrella to do 20

to 22 or more individual phase II trials. So that trials will—they're open now, but they will close quickly. It's not going to be that long—we won't wait until the end of the accrual phase for the study to get information out to public. Warren, do you want to say anything?

KIBBE: That's right as we start to close different arms we'll make data available. Our thought now is it will flow to the Genomic Data Commons, and will be available there. How quickly will we get it into the Genomic Data Commons? It won't be there until June 2016, because the Genomic Data Commons doesn't open until June of 2016. That would be the earliest the data is available there.

JACKS: That is important clarification in answer to your question, because it doesn't sound like data availability is dependent on publication. Closing trials rather than completion, and access by the data commons.

Kevin is asking me if that's codified. It sounds to me like it's a plan under discussion. But your suggestion I think would be that it should be codified somewhere.

GRAY: Doug, I was wondering if you or Warren could say more about the DoE interactions. In particular, what is DoE's role in this? Are they just providing compute cycles or are they actually scientifically engaged in algorithm development and things like that?

KIBBE: With respect to the DoE, I think this is a really great opportunity for us to have a partnership with them. Both an intellectual and a resource partnership. I don't think it would be in NCI's or the cancer community's best interest if we just duplicated their resources or tried to duplicate their expertise.

What I do think this partnership gives us the ability to do is to bring resources and the expertise that they have and make it more relevant for our community. So that's really the basis of this initiative, bringing the two groups and having us learn from each other and hopefully having us partner over the long time.

GRAY: But that didn't quite answer the question. So curious what resources DoE is actually putting into this? Historically, they have not been terribly willing to invest in human research, or at least in a reduced level.

So I'm curious to whether or not DoE is contributing scientific resources to this, or are they making compute cycles available?

KIBBE: It will most definitely be partnership with scientists in the DoE as well as the NCI. How many? I think that's still under discussion.

LOWY: There is considerable interest on the part of the Department of Energy. Warren and I met with Sec. [Ernest] Moniz a couple of months ago and we will meet again in two weeks, and both times were at his request.

JACKS: I had a question about the R50, and this might be for Dinah to address. It states the grant for the research specialists will be used to basically offset the salary that is paid on NCI-funded cancer research. I'm confused about what that means exactly. Is it expectation the individual is already supported on existing grants and therefore their salary is shifted to new award? And their salary on the old award will be what? Shifted over?

So it's a net no gain, just a shifting of the dollars from one pot to another? So that basically answers my question…

MACK ROACH [NCAB member and director of the Particle Therapy Research Program & Outreach at the University of California, San Francisco]**:** One thing related to budget stuff, I want to appreciate and say that this is one of the best pamphlets that I have seen put out. So to summarize and state what the budget is looking like for the fiscal year 2017, I think it looks very positive.

We have had a lot of funding issues over the number of years. It's nice to see something that talks about more money and giving people some ideas about where the money is being spent. So I wanted to say somebody did a good job of this brochure.

LOWY: A lot of people put in a lot of work, but especially Rick Manrow is the person who was responsible for a lot of the writing.

We are already thinking about the FY 18 bypass budget request. One feature in FY 17 is the notion of trying to get sustained increase in NCI budget. And one of the features that we are planning to put in to the FY 18 budget is some of the important projects that we could consider embarking on or really doing at a much bigger scope if there were more funding.

We're going to be asking people for input about the kinds of projects, etc., so that we are hopeful that the FY 18 bypass budget maybe you will say a year from now, "That's even better than 2017!"

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In Brief

Choi Named OncoDermatology Chief at Northwestern Memorial

JENNIFER NAM CHOI was named chief of the Division of OncoDermatology at **Northwestern Memorial Hospital** and associate professor in the Department of Dermatology at Northwestern University Feinberg School of Medicine. Choi will also join the melanoma team at Northwestern Medicine.

The Division of OncoDermatology is comprised of dermatologists who specialize in treating the mucocutaneous complications of cancer treatments and comprises one of five units within Northwestern Medicine's Skin Cancer Institute of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Specifically, Choi's team provides care for skin, mucosal, hair and nail toxicities in patients undergoing cancer treatment, including chemotherapy and radiation. Her team also manages toxicities that may arise as a result of stem cell or solid organ transplantation—utilizing its graft-vs-host disease program, the skin cancer surveillance initiative for high-risk patients and Northwestern Memorial's extracorporeal photopheresis unit.

Choi was the founder and director of the Yale Oncodermatology Clinic at Yale School of Medicine since 2008, and also served as the Melanoma Unit Disease Team co-leader at the Yale Cancer Center since 2009.

ROBERT HAUSER was named vice president of clinical analytics at **Cancer Treatment Centers of America** Medicine & Science.

Hauser will direct the development of a analytics program to support enhancements in quality of care, clinical research and clinical innovation. In this role, he will assess the organization's clinical analytic and data needs, design strategy and tactics to meet those needs, and lead implementation of analytic and reporting strategies.

Hauser most recently served as senior director of the American Society of Clinical Oncology's Quality and Guidelines Department where he managed the development of ASCO's CancerLinQ project. Previously, he was the director of operations and informatics at the International Oncology Network. Additionally, Hauser also served as vice president and chief operating officer of Geriatric Oncology Consortium Inc.

MIA LEVY was named director of Cancer Health Information and Strategy at **Vanderbilt-Ingram Cancer Center**. Levy is the Ingram Assistant Professor of Cancer Research and director of Cancer Clinical Informatics at the center.

In this newly created role, Levy will conceptualize and supervise the development of new informatics tools to support precision cancer medicine, data analytics and cancer care coordination.

Levy worked as co-developer of My Cancer Genome, an online medical decision support tool for cancer care hosted online by VICC.

CITY of HOPE announced three recent hires.

Bart Roep joined City of Hope as chair of the Department of Diabetes Immunology within the Diabetes & Metabolism Research Institute.

Roep served as head of the Division of Autoimmunity and professor of medicine, diabetology, immunopathology and immune intervention therapy at Leiden University Medical Center in the Netherlands. He also served as director of the Netherlands' National Diabetes Expert Center on Immunoprotection.

A recognized authority on multiple aspects of type 1 diabetes, including the potential for vaccine therapy to cure the disease, Roep has been honored with the JDRF Gerold & Kayla Grodsky Basic Research Scientist Award 2015 and the Minkowski Award for T1D Scientific Excellence 2004, the most prestigious national and European awards in diabetes.

Veronica Jones joined City of Hope as an assistant clinical professor in the department of surgery, specializing in breast surgery.

Jones was an assistant professor in the department of surgery at Emory University. At Baylor, Jones was honored as chief resident of the year. In 2014, she completed a breast surgical oncology fellowship at Emory University.

Daneng Li, joined City of Hope as an assistant clinical professor in the department of medical oncology and therapeutics, specializing in geriatric oncology, and GI oncology

Li receive his medical doctorate from Weill Cornell Medical College in New York, before pursuing an internship and residency in internal medicine at New York-Presbyterian Hospital/Weill Cornell Medical Center. He recently completed a hematology/oncology fellowship at Memorial Sloan-Kettering Cancer Center in New York City.

DAVID FLOCKHART, board member of **The Personalized Medicine Coalition**, died Nov. 26.

Flockhart helped establish a foundation for personalized medicine by developing the P450 Drug Interaction Table, which provides information on how an individual will metabolize certain drugs.

Flockhart, who served as the director of the Indiana Institute for Personalized Medicine at Indiana University, had been elected to PMC's board of directors just months before he passed away of glioblastoma multiforme on Thanksgiving.

PMC Board Chair William Dalton said Flockhart was an extraordinary leader for the field.

"Dave Flockhart was a unique individual in many ways, combining outstanding scientific skills with integrity and compassion," Dalton said. "He will be remembered as an impactful scientist, clinician and mentor dedicated to the advancement of personalized medicine to improve the lives of patients everywhere. Indeed, Dave was truly inspirational in his ability to learn and ultimately teach us all in dealing with his own health challenges. He will be sorely missed."

In an interview published in September in the fall issue of PMC's newsletter, Education + Advocacy, Flockhart described his experience receiving personalized care. He emphasized the importance of thoughtful interactions with patients.

"It is the simple act of caring that really matters," he said. "Of course, the advances of knowing what drugs my cancer is more likely to respond to are important. The skill of my surgeon is important, but what matters most when you are undergoing treatment is a kind word, a touch, the simple act of caring."

Prior to joining Indiana University in the summer of 2001, Flockhart had served as the Francis Cabell Brown Chair, chief of the Division of Clinical Pharmacology and director of the Pharmacogenetics Core Laboratory at Georgetown University Medical Center.

A native of Edinburgh, Scotland, Flockhart obtained a Ph.D. from the Welsh National School of Medicine and an M.D. from the University of Miami School of Medicine.

FOX CHASE CANCER CENTER - Temple Health formed a partnership with **Accutest Research Laboratories** for joint work on clinical trials.

The partnership aims to offer a research platform to conduct clinical trials in the United States, India, Southeast Asia and Latin America. Representatives of both organizations signed a non-binding memorandum of understanding on Nov. 10 in New Delhi.

Accutest was founded in 1998, and offers end-to-end services to pharmaceutical and biotechnology companies. Its services include phase I bioavailability/bioequivalence studies, phase II - IV clinical development services and biosimilars services, covering clinical operations, clinical data management, pharmacovigilance, and medical writing services.

MANIPAL HOSPITALS' corporate and teaching facilities in India will adopt **IBM Watson for Oncology**, a cognitive computing platform that analyzes data to identify evidence-based treatment options. This will be the first deployment of Watson in India.

Watson for Oncology was developed by IBM in concert with Memorial Sloan Kettering Cancer Center. To date, Watson for Oncology has ingested nearly 15 million pages of medical content, including more than 200 medical textbooks and 300 medical journals. This year alone, nearly 44,000 oncology research papers have been published in medical journals around the world. This amounts to nearly 122 new papers published every day.

THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY published a new template that standardizes and streamlines the creation of patient-focused plans for long-term cancer survivor care following radiation therapy.

The template and related research papers, "Development of a Standard Survivorship Care Plan for Radiation Oncologists" and "U.S. Radiation Oncology Practice Patterns for Post-Treatment Survivor Care," are published in Practical Radiation Oncology, the official clinical journal of ASTRO.

The template was developed to coordinate post-treatment care for cancer survivors among the various contributors to their care, including primary care providers and oncology specialists, as well as patients.

The framework also helps practices meet new accreditation requirements set by the American College of Surgeons Commission on Cancer. In response to a 2006 recommendation from the Institutes of Medicine that cancer patients be provided with a survivorship

care plan following treatment, CoC issued a mandate that cancer programs provide SCPs for all curative cancer patients by 2019 to maintain accreditation.

The new requirement may necessitate changes for the majority of radiation oncology programs, according to data from a March 2014 survey of ASTRO members. The survey found that only 40 percent and 19 percent of respondents used SCPs for curative and palliative patients, respectively. Primary barriers to implementation included cost and the lack of a standardized, comprehensive SCP framework suited to patients who received RT. Nearly 80 percent of the RT providers that reported using SCPs relied on a framework developed internally within their practice, indicating that different patients may receive different types of information depending on where they receive treatment.

"This two-page template facilitates consistency in SCPs across the discipline and also reduces the time and effort required by providers to complete each individual plan," said Ronald Chen, an associate professor in radiation oncology at the University of North Carolina at Chapel Hill and lead author on the manuscript that includes the template.

"The field of radiation oncology has a long tradition of creating treatment summaries for each patient, even before the Institute of Medicine recommended survivorship care plans in 2006. This radiation-oncology specific template will serve a dual purpose as both a traditional radiation oncology treatment summary and a plan for survivorship care that meets CoC requirements – thus reducing the burden on radiation oncologists from having to create two documents for each patient."

Chen was the chair of ASTRO's Clinical, Translational and Basic Science Advisory Committee, the group that examined current adoption levels of SCPs and developed the template to standardize them in the future.

WEST CANCER CENTER celebrated the grand opening of its East Campus location with a ribbon cutting ceremony Nov. 17.

The 123,000 square foot facility combines West Cancer Center's multispecialty services and clinical research program all at one location.

"This marks another milestone in the transformation of how we care for and treat our patients," said Erich Mounce, CEO of West Cancer Center.

"By physically combining the forces of our multidisciplinary specialty teams into one facility, we are creating an environment that truly fosters collaboration and produces a unique understanding of what each specialty requires, allowing everyone to perform at their highest level."

The opening is a result of a partnership between Methodist Healthcare, the University of Tennessee Health Science Center, and West Clinic, who joined together in January 2012 to form West Cancer Center.

THE NATIONAL HEALTH CARE ANTI-FRAUD ASSOCIATION today presented its Investigation of the Year Award to a team of federal agencies together with a private health insurer for their collaborative work on the case of *United States of America v. Farid Fata, MD.*

This investigation involved a leading hematologist-oncologist in Michigan who misdiagnosed and mistreated hundreds of his patients for conditions they did not have, including cancer, in order to maximize billing to Medicare and private insurance.

Over the course of four days, the initial tip was received, allegations were verified, and search warrants and criminal complaints were prepared, resulting in Fata's arrest.

On July 10, Fata was sentenced to 45 years in federal prison and ordered to forfeit $17.6 million for violating the trust of 553 patients and for submitting approximately $34 million in fraudulent claims. At his sentencing, U.S. District Judge Paul Borman said, "This is a huge, horrific series of criminal acts that were committed by the defendant," and then said that Fata "practiced greed and shut down whatever compassion he had."

The awardees are: the Fraud Section of the Department of Justice Criminal Division; the Office of Investigations under the Inspector General of the Department of Health and Human Services; the Criminal Investigation department of the Internal Revenue Service; U.S. Attorney's Office for the Eastern District of Michigan; the FBI Detroit Field Office; and Blue Cross Blue Shield of Michigan Corporate and Financial Investigations.

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Funding Opportunity

Debbie's Dream Foundation

Debbie's Dream Foundation: Curing Stomach Cancer launched two research grants totaling $200,000 for the 2015-2016 grant cycle. A Career Development Award for $150,000 and a Young Fellowship Grant for $50,000 are being offered.

The grants will be administered by the American Association for Cancer Research. The DDF Gastric Cancer Fellowship Grant is geared toward postdoctoral and clinical researchers, while the Career Development Award is geared toward junior faculty who have completed their most recent doctoral degree or medical residency within the past eleven years. Both grants aim to involve those who conduct gastric cancer research and want to establish a successful career path in this field.

"For the third year in a row, we are thrilled to fund gastric cancer research. Each year we have doubled the amount award and the total we have authorized for research is $350,000," said DDF President and Founder Debbie Zelman.

The grants are for basic, translational, and clinical research in stomach cancer and are available to scientists and clinicians at various career levels.

More information about the grants is available on the Debbie's Dream website.

Drugs and Targets

FDA Approves Opdivo Injection For Renal Cell Carcinoma

FDA approved Opdivo (nivolumab) injection for the treatment of patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy.

In the CheckMate -025 trial, patients treated with Opdivo achieved a median OS of 25 months (95% CI: 21.7-not estimable) versus 19.6 months (95% CI: 17.6-23.1) for everolimus, a current standard of care (HR: 0.73; [95% CI: 0.60-0.89; p=0.0018]), based on a prespecified interim analysis.

In the study, the safety profile was consistent with prior Opdivo studies.

"This is the fifth approval for Opdivo across three distinct tumor types. This latest approval reflects our commitment to delivering on our promise to provide cancer patients with a potential for long-term survival," said Francis Cuss, executive vice president and chief scientific officer at Bristol-Myers Squibb, Opdivo's sponsor. "We believe our pioneering approach to Immuno-Oncology is driving change in how cancer may be treated."

The U.S. approval was based on data from CheckMate -025, an open-label, randomized phase III study which demonstrated a median OS benefit of 25 months (95% CI: 21.7-NE) compared with 19.6 months (95% CI: 17.6-23.1) for everolimus (HR: 0.73; [95% CI: 0.60-0.89; p=0.0018]).

FDA previously granted Breakthrough Therapy Designation to Opdivo for advanced RCC patients treated with prior anti-angiogenic therapy, also based on positive results from the CheckMate -025 study.

"This approval of Opdivo represents a major milestone for the kidney cancer community," said William P. Bro, chief executive officer and patient coordinator, Kidney Cancer Association. "We thank Bristol-Myers Squibb and the FDA for working swiftly to bring this important new treatment option and potential for extended survival to patients."

The European Commission granted marketing authorization for Kyprolis (carfilzomib) in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Kyprolis, sponsored by Amgen, is the first irreversible proteasome inhibitor approved in the European Union for use in combination treatment of patients with relapsed multiple myeloma.

"In clinical studies, approximately one out of three patients achieved a complete response or better on the Kyprolis in combination with lenalidomide and dexamethasone arm, which is three times more frequent than in the lenalidomide and dexamethasone arm," said Prof. Meletios Dimopoulos of the National and Kapodistrian University of Athens School of Medicine. "In addition, the regimen provided patients with more than two years without disease progression. These results are significant for patients with relapsed multiple myeloma, who are faced with worse outcomes each time they experience a relapse."

The EC approved Kyprolis based on data from the phase III ASPIRE trial. The study showed that patients treated with Kyprolis in combination with lenalidomide and dexamethasone had increased median time to progressive disease or death by 8.7 months compared to patients treated with lenalidomide and dexamethasone.

The median progression-free survival was 26.3 months in the KRd arm compared to 17.6 months in the Rd arm (HR: 0.69; 95% CI: 0.57 to 0.83; p=0.0001).

The most common adverse events in the Kyprolis arm included pneumonia, myocardial infarction and upper respiratory tract infection. Discontinuation of treatment due to AEs occurred in 15 percent of patients in the KRd arm versus 18 percent of patients in the Rd arm.

Kyprolis received an accelerated assessment from the European Medicines Agency, and orphan drug designation in 2008.

The European Medicines Agency accepted a marketing authorization application for review of anamorelin HCI, a novel, orally active selective ghrelin receptor agonist under development for the treatment of anorexia, cachexia, or unintended weight loss in non-small cell lung cancer patients. Anamorelin is being developed by Helsinn.

Ghrelin is an endogenous peptide primarily secreted by the stomach. Upon binding to its receptor, ghrelin stimulates multiple pathways in the positive regulation of body weight, lean body mass, appetite and metabolism. Anamorelin is an investigational agent that has not yet been approved by any regulatory authority.

MD Anderson Cancer Center and Boehringer Ingelheim announced a collaboration focused on developing innovative medicines for pancreatic ductal adenocarcinoma.

The collaboration will focus on identifying and developing therapeutic concepts in novel target areas as well as identification of biomarkers that can accurately identify patients who would respond to potential new therapies.

"This partnership is a perfect match because it combines MD Anderson's outstanding capabilities in preclinical concept validation and clinical testing with Boehringer Ingelheim's strength in developing innovative medicines," said Clive Wood, senior corporate vice president of Discovery Research at Boehringer Ingelheim.

Morphotek Inc., a subsidiary of Eisai Inc., entered into an agreement with the Targeted Alpha Therapy Group at the University of Gothenburg in Sweden to collaborate on the research and development of farletuzumab as an alpha therapy vector being studied for radioimmunotherapy in ovarian cancer.

Farletuzumab is an investigational humanized monoclonal antibody that binds to folate receptor alpha, a protein which is highly expressed in ovarian carcinoma but largely absent from normal tissue.

In radioimmunotherapy, mAbs are attached to radioisotopes that may potentially deliver highly cytotoxic radiation in a targeted and more direct way to relevant cancer cells. The use of alpha emitters, in contrast to beta emitters, may potentially allow for the killing of only targeted cells binding with the vector due to the short alpha particle track. This collaboration will initially investigate the use of farletuzumab as an alpha therapy vector in preclinical laboratory studies, followed by the overall objective, which is to investigate in clinical trials the safety and efficacy of alpha-radiolabeled farletuzumab in women who enter remission upon completion of first-line treatment.

Farletuzumab is currently being tested in a clinical study in first-relapsed, platinum-sensitive ovarian cancer patients with low CA125 levels. The double-blind, randomized-controlled study is designed to prospectively evaluate the clinical effects observed in the previously conducted phase III trial in the pre-specified subset of patients treated with farletuzumab exhibiting low CA125 levels.

The TAT Group's research activities will be coordinated by various departments at the Sahlgrenska Academy, University of Gothenburg, under the direction of Associate Professor Per Albertsson, an oncologist at Sahlgrenska University Hospital.

Roche and Upsher-Smith Laboratories Inc., through its wholly-owned U.K. subsidiary Proximagen Ltd., announced a worldwide agreement for the further development of a novel, oral small molecule inhibitor of Vascular Adhesion Protein 1, a cell-adhesion molecule that may be effective in the treatment of inflammatory disease. The VAP-1 inhibitor is currently in phase II clinical development.

Under the terms of the agreement, Roche is granted a worldwide exclusive license to develop and commercialize the compound. In a novel collaboration model, Proximagen and Roche will conduct additional phase II studies to further define the therapeutic potential of the VAP-1 inhibitor. Based on these data, Roche will assume responsibility for late stage development and worldwide commercialization.

Proximagen will receive an upfront payment, along with downstream development, regulatory and sales milestones. In addition, Proximagen will also receive tiered royalties on net sales of a potential future product containing the molecule.