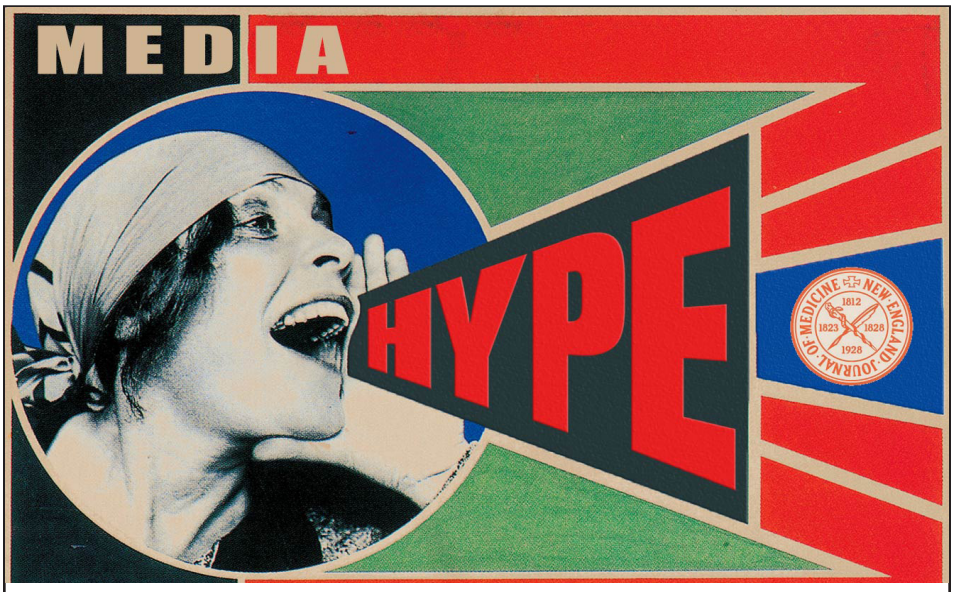
THE CANCER LETTER

March 18, 2016 • www.cancerletter.com • Vol. 42 No. 11



Brigham Doc's NEJM Paper Decries Morcellation's Demise, But How Did She Get Confidential Patient Information?

By Matthew Bin Han Ong

Clearly, Lisa Rosenbaum wanted to trigger a heated discussion—but not of the sort she ended up with.

Rosenbaum, a national correspondent at the New England Journal of Medicine, focused on the demise of power morcellation, a once widely used gynecological procedure, which in some cases ended up disseminating undetected uterine sarcomas.

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Capitol Hill

Senate Bill Gives FDA More Control Over Its Hiring, Salaries and Structure

By Conor Hale

The FDA and NIH Workforce Authorities Modernization Act was introduced in the Senate by Republican and Democratic leaders of the health committee. The bill aims to help FDA and NIH "attract top talent during this exciting time in science."

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Slamming the Door

Part VIII - A Conversation with DePinho

By Paul Goldberg

The $18 million never made it from Austin to Houston.

MD Anderson's initial stance was to deflect all CPRIT-related questions to CPRIT, but this didn't make the controversy go away. So, the cancer center suggested that the grant undergo scientific review, as well as commercial.

(Continued to page 7)

NEJM Paper Decries Demise of Power Morcellation

(Continued from page 1)

In a paper published in the March 10 issue of the journal and titled "N-of-1 Policymaking—Tragedy, Trade-offs, and the Demise of Morcellation," Rosenbaum alleges that Amy Reed, a high-profile opponent of power morcellation, had stage IV cancer before her hysterectomy.

What was Rosenbaum's basis for saying this with no equivocation? After all, the initial stage of Reed's disease was never made public and was generally presumed to be early-stage. Alas, Rosenbaum's paper is mum on sourcing.

The only footnote in vicinity of this bit of personal health information takes the reader to the American Cancer Society's compilation of cancer statistics. Writes Rosenbaum: "The masses turned out to contain foci of leiomyosarcoma (LMS), a rare, aggressive cancer that has a 5-year survival rate of 63% when diagnosed at stage I. Reed's LMS was stage IV, so her likelihood of surviving 5 years was only about 14%."

Had Rosenbaum been a cub reporter at a local newspaper, rather than a Harvard cardiologist writing for one of the world's most esteemed general medical journals, her editor would have demanded that she either (1) cite her source, or (2) explain why the source couldn't be revealed, and (3) be dead-sure of her facts.

Actually, appearances in this case are even more perilous. Rosenbaum practices at Brigham & Women's Hospital, the very institution where Reed had her ill-fated hysterectomy, and which Reed is now suing. Of course, the question of staging is important to Rosenbaum's article. If Reed indeed had stage IV disease at the time of her initial surgery, her "N-of-1" advocacy would be based on the wrong "1." Presumably, the issue of staging would be important to lawyers, too.

Contacted by The Cancer Letter, Rosenbaum did not respond to questions.

On March 14, as a direct consequence of the NEJM story, Reed filed a complaint under HIPPA, the Health Insurance Portability and Accountability Act, with the Office of the Massachusetts Attorney General and the HHS Office of Civil Rights.

"Dr. Rosenbaum has written a recent article for the NEJM, which includes statements referring to medical care that I received explicitly at BWH in conjunction with DFCI," Reed wrote in the complaint. "Based on the specific content of these statements, I am concerned that my medical records have been accessed by either Dr. Rosenbaum directly, as a Brigham physician, or by discussions she held with my treating physicians—both would be illegal because I never provided consent for such access to Dr. Rosenbaum.

"Again, Dr. Rosenbaum's specialty falls outside of care that I received and she would have had no clinical reason to access any of my HIPAA-protected medical information—other than for the purpose of publicity," wrote Reed, formerly an anesthesiologist at Beth Israel Deaconess Medical Center.

Reed's husband, Hooman Noorchashm, said Rosenbaum's allegation that his wife had stage IV sarcoma in October 2013 is incorrect.

"This is an inaccurate misrepresentation, particularly because the clinical data—including a lung biopsy done to rule out metastatic disease by Dr. Scott Swanson [chief surgical officer at Brigham] in early 2014—proves otherwise," said Noorchashm.

NEJM officials declined to respond to The Cancer Letter's questions on sourcing, citing an "ongoing investigation prompted by a complaint filed with a government agency."

In a statement, Brigham officials said that "the hospital's Privacy Office has concluded the audit of Reed's record and has determined that Rosenbaum did not access Dr. Reed's record."

Noorchashm, formerly a cardiothoracic surgeon at Brigham, said that, based on his direct knowledge of the information systems at the institution, a person can access the radiology imaging archive system without leaving an electronic fingerprint. Cafeteria conversation, too, can come into play, he said.

"We hope this will be vetted by the [Massachusetts attorney general's office] and the HHS OCR

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Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $420 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.

investigations," Noorchashm said.

Reed and Noorchashm asked Rosenbaum directly whether she accessed Reed's files.

"I did not read Dr. Reed's medical records, nor did I discuss her care with any of her treating physicians," Rosenbaum wrote in a March 14 email to the couple. "The stage of her cancer has been reported in several media outlets."

Reed said no news publication had reported the stage of her cancer at the time of her surgery at Brigham.

"She's like, 'Oh, you know, it was published.' No, it actually wasn't, because it's not true," Reed said. "At best, I think it's irresponsible journalism, and that's not even getting at what the message of this paper is."

"Availability Entrepreneurs"

In the NEJM article, Rosenbaum characterized Reed and Noorchashm as "availability entrepreneurs" who "exploit reporters eager to break stories of transgression."

Rosenbaum writes that FDA used "poor data" to engage in "N-of-1 policymaking," because of public outrage from widespread media attention that "exaggerated the risk of LMS."

FDA disagrees. In response to Rosenbaum's allegations, the agency said it doesn't use N-of-1 anecdotes, low-quality data, or media hype in its policymaking decisions.

Contacted by The Cancer Letter, the agency said it stands by its actions.

"No, the FDA's primary concern is the safety and well-being of patients," an FDA spokesperson said. "The FDA bases its decisions on what is in the best interest of public health, carefully balancing both the benefits and risks of a product. The FDA evaluated the available data at the time and determined that it was of sufficient quality and reliability to support our November 2014 decision."

In her conflict-of-interest form, Rosenbaum disclosed her NEJM position as one of the "relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work."

However, in the same section—Section 5 of the form created by the International Committee of Medical Journal Editors—she does not mention her relationship with Brigham.

This is fine, NEJM officials said. "In the interest of transparency, Dr. Rosenbaum discloses her employment as a BWH physician in the fourth paragraph of her article," an NEJM spokesperson said to The Cancer Letter. "Readers do not need to visit a separate disclosure form to learn this."

Rosenbaum and NEJM should have explicitly disclosed any potential conflicts or the appearance of one, said Arthur Caplan, the Drs. William F. and Virginia Connolly Mitty Professor of Bioethics and director of the Division of Medical Ethics at New York University Langone Medical Center.

"It's a potential institutional conflict; she's working in a place that's getting sued," Caplan said to The Cancer Letter. "You'd want to know about that, because of her special access to information or sources that may not otherwise be available to the general media covering this issue. I think the disclosure of those things should've been better than it was.

"There's enough there that I think it belongs in a disclosure form, it should've been something that got broader attention in the piece, either by her or at the suggestion of the editor. When there are lawsuits flying, insider access is important to know—it's something that readers or a reasonable person would want to know about. They should've done more to disclose, either the author or the editor. It could well get a note. In general, you'd want to say something about the source.

"Not everything demands disclosure by the reporter to the same degree, but this one—you've got to really think hard when half the American legal profession is suing each other."

The NEJM editors have an obligation to insure the authenticity and accuracy of Rosenbaum's information, said Meg Kissinger, an investigative health reporter for the Milwaukee Journal Sentinel, a 2009 Pulitzer Prize finalist for investigative reporting, and a two-time George Polk Award winner for medical and environmental reporting.

"For their own sake, they have to ensure that disclosures are made, so that there is no question for the readers about the point of view," Kissinger said to The Cancer Letter. "Journalists have their code of ethics to follow; doctors, of course, have the medical code of ethics. This doctor-journalist has a double set of ethical considerations. What distinguishes her is that she technically does have access, that's another reason why her association should've been disclosed.

"Sometimes, as journalists, sources give you stuff, but then it's your job to verify their authenticity. For her own sake, she should have attributed her information. She could've saved herself some headaches there. It would seem to me an abuse of her position if she did indeed get the information by virtue of her being a doctor."

The manner in which Rosenbaum notes her

Brigham relationship is insufficient, said Roy Poses, a clinical associate professor at the Alpert Medical School at Brown University and president of the Foundation of Integrity and Responsibility in Medicine.

"In the article, the author, Dr. Rosenbaum, says that she 'joined the faculty' of Brigham, again, the hospital that is involved in this legal controversy," Poses said to The Cancer Letter.

"I cannot tell from that simple phrase, whether Dr. Rosenbaum does some unpaid teaching at the hospital or voluntary unpaid care of indigent, or on the other hand, whether she works for the hospital for a salary. It would seem to me that whether she has in fact a significant financial relationship or not might be relevant to understanding whether she actually has a conflict of interest in writing this article."

Rosenbaum's financial relationship with Brigham is unclear—the hospital declined to provide information on Rosenbaum's title and whether she is a full-time faculty member, citing personnel policies.

"I can see that the hospital would not want to reveal her salary, if in fact she has one, and that has privacy implications," Poses said. "But I don't understand why the hospital would not be able to simply tell you whether or not she is employed there and in what capacity."

At least two suits claiming medical malpractice have been filed against Brigham—one by Reed and Noorchashm, and the other by Richard Kaitz, whose wife, Erica, died Dec. 7, 2013 from metastatic leiomyosarcoma, nearly two months after Reed received her cancer diagnosis at Brigham (The Cancer Letter, Nov. 21, 2014).

Kaitz and Reed are also in product liability litigation against Karl Storz, the manufacturer of the power morcellators used at Brigham. Of 100 or so lawsuits against Johnson & Johnson subsidiary Ethicon—which manufactured nearly three quarters of the devices on the market—about 70 have been settled, according to The Wall Street Journal.

Congress, FBI and the Government Accountability Office have launched probes into issues of hospital compliance with adverse outcomes reporting laws and patient safety regulations (The Cancer Letter, Dec. 18, 2015).

"The work has just gotten underway so it is very early in the process," a GAO spokesperson said to The Cancer Letter. "Some of the first steps will be to determine the scope of what will be covered and the methodology to be used."

Observers: Rosenbaum's Confusing Arguments

Reed and Noorchashm launched an aggressive campaign in late 2013 against power morcellation—over 300 patients and families have come forward claiming harm. Their advocacy led to FDA restrictions and a black box label on the use of power morcellators, finding that one in 350 women undergoing hysterectomies or myomectomies have an unsuspected uterine malignancy. Hospitals banned the surgery, and the agency's final guidance largely ended insurance coverage for the procedure.

Rosenbaum characterization of FDA's decision on power morcellators as based on an N-of-1 is inaccurate, NYU's Caplan said.

"There's been lots of allegations of safety issues," Caplan said to The Cancer Letter. "Now, you could say this is a case of 'N-of-1' high visibility policymaking, in which Dr. Reed and her husband are both doctors, they've really lobbied hard to get attention to the issue and it's a case that has played a prominent role, but I wouldn't say it's 'N-of-1.'"

"I don't think the FDA, in my experience, would do 'N-of-1' policymaking. 'N-of-1' would get their attention as to, 'Is there a problem?' but the agency always wants to push further and establish, 'Is there a pattern, is there an outlier?' They're not just going to say, 'Oh okay, we had an adverse event, and that puts us in a position to make policy.' They are always going to examine and go further.

"I know in the fight that there certainly have been exchanges back and forth about other cases. There are certainly red flags flying around which say, 'Maybe we don't leave this to just doctor-patient negotiation, we've really got to establish what the risk profile is here.' That's the FDA's job, and I think it's all going to come out in litigation."

Brigham physicians knew of at least three or four cases before Reed, said Kaitz, a Boston real estate attorney.

"N-of-1? That's absurd. All you have to do is look at the collage of pictures of all the victims. That's ridiculous. For the Brigham, it wasn't an N-of-1," Kaitz said to The Cancer Letter. "FDA listened to lots of different parties, lots of different experiences. I personally have been in touch with 20 to 30 victims, families in only the last year or two, so God knows how many there were before that—they've done the procedure for 15 to 20 years. No, it's not N-of-1 policymaking at all.

"The media have not been exploited, absolutely not. I am an extremely reluctant participant in this public discussion, because it's just not the way I operate. At

the same time, articles like this and some of the actions that Brigham has taken, you can't just sit back and watch them.

"I personally am happy with what FDA has said—the practice of morcellation as we knew it doesn't exist today. Certainly Amy and Erica would not be subject to morcellation today."

In a study by Brigham physicians Michael Muto and Michael Seidman published November 2012 in PLOS ONE, the authors identify four patients—out of 1,091—who showed evidence of peritoneal dissemination of leiomyosarcoma after undergoing power morcellation. Three of the four patients died, with an average post-diagnosis survival of 24.3 months. It is not publicly known where the four patients were treated.

Robert Lamparter, a retired pathologist, alerted Ethicon about potential problems with morcellators in 2006 (The Cancer Letter, Nov. 20, 2015).

Rosenbaum's arguments about the data and about the efficacy and safety of power morcellation are "confusing," because she doesn't provide data about the benefits, said Poses.

"Where to draw a line to say a particular treatment is safe is not always easy; the FDA made a decision based on recent information that this device was not safe," Poses said. "I'm not sure that the discussion of the data in Dr. Rosenbaum's article helps with the decision.

"She talks about the data concerning the possible harms of power morcellation and argues that that data comes from relatively low-quality studies, not randomized, controlled trials, and that it is hard to tell the actual rate of harms, in particular, the dissemination of cancer. On the other hand, Dr. Rosenbaum implies that the benefits of power morcellation are well known.

"She writes initially that power morcellation allows the treatment of fibroids to be 'done more efficiently and effectively,' she later implies that power morcellation is less invasive, leads to quicker recovery, avoids income loss, and furthermore, reduces the likelihood of pulmonary embolus, wound infection, or hemorrhage.

"However, she doesn't provide any data about these ostensible benefits. A quick search suggested that there are no good randomized, controlled trials that assessed benefits. Her argument that we have abandoned a beneficial treatment based on poor quality and perhaps exaggerated the data about its harms—that does not seem to be supported by any clear data about its benefits."

Poses said he is surprised that the NEJM would publish Rosenbaum's article at all.

"The NEJM is perhaps the most prestigious, most highly regarded English-language medical journal in the world," Poses said. "It is, in many cases, viewed as the standard for scholarly medical journals. I am a bit surprised that it published a commentary by its own national correspondent that appears to make an argument—about benefits and harms of treatment and policymaking about treatment—that does not have a clear discussion of the data that support or fail to support either the benefits or the harms of the treatment."

Rosenbaum's parallels make no sense, Poses said.

"Toward the end of the article, the author, Dr. Rosenbaum, writes that 'Noorchashm insists that it's unethical to consider morcellation's majority benefit when some individual patients may face such serious adverse consequences.' The article by Dr. Rosenbaum never really goes over the data that does or does not suggest 'majority benefit,'" Poses said. "Then, Dr. Rosenbaum goes on to say, 'such reasoning could easily apply to giving ACE inhibitors to patients with heart failure…' I fail to understand the parallel.

"There were multiple, large, reasonably well done randomized controlled trials of ACE inhibitors for heart failure," said Poses, who adds that he is familiar with research on ACE inhibitors. "These trials show clear survival benefits and relatively infrequent mild to moderate adverse effects. There is no parallel because, again, there were large trials, the benefits were clear, and they included increased survival, and the adverse effects were reasonably clear and did not appear to come close to outweighing the benefits.

"So I fail to understand the argument by Dr. Rosenbaum, and I feel it makes the article even more confusing."

FDA: Media Hype, 'N-of-1' not Factors in Policymaking

In a statement to The Cancer Letter, FDA said it relied on data that was of "sufficient quality and reliability" to support its final November 2014 guidance on power morcellation.

The full text of FDA's response follows:

The FDA reviewed the related data, including adverse event reports, published and unpublished literature, product labeling and other materials to determine the nature and significance of this issue. As part of its review, the agency considered the benefits and risks of the use of these devices.

The FDA review concluded that there is a risk of spreading unsuspected cancerous tissue beyond the uterus when using laparoscopic power morcellation

for hysterectomy or myomectomy in women with uterine fibroids.

The literature has reported that women are often told that the risk of having an unsuspected leiomyosarcoma is 1 in 10,000, a relatively small risk; however, based on the FDA's analysis of available data, the FDA believes the estimated risk of unsuspected uterine sarcoma in women undergoing hysterectomy or myomectomy for the treatment of uterine fibroids is closer to 1 in 350. As a result, the FDA issued a safety communication in April 2014 discouraging the use of laparoscopic power morcellation for the removal of the uterus (hysterectomy) or uterine fibroids (myomectomy) in women.

While others have produced different risk estimates, the general consensus among the clinical community is that the risk is higher than what was previously understood. The FDA also wants to ensure that women considering the procedure know that power morcellation can increase the risk of spreading cancerous tissue in women with undetected cancer in the uterus.

The FDA evaluated the available data at the time and determined that it was of sufficient quality and reliability to support our November 2014 decision. The FDA's analysis of available information indicated that the risk of having an unsuspected uterine sarcoma, a type of uterine cancer, in a woman undergoing surgery for presumed fibroids is approximately 1 in 350 women. If laparoscopic power morcellation is performed in these women during the removal of the uterus (hysterectomy) or fibroids (myomectomy), there is a risk that the procedure will spread the cancerous tissue. An outside panel of experts also felt that the risk of unsuspected uterine cancer should be included in the product labeling, and that it was critical that doctors discuss the risks and benefits of all options with their patients.

The FDA's primary concern is the safety and well-being of patients. The FDA believes that it is possible to reduce the risk of unsuspected cancer spread by warning against the use of laparoscopic power morcellation in the vast majority of women undergoing myomectomy or hysterectomy and clarifying the small patient population for whom morcellation may be an acceptable therapeutic option.

The FDA bases its decisions on what is in the best interest of public health, carefully balancing both the benefits and risks of a product. The Agency has recommended that health care providers thoroughly discuss the benefits and risks of all treatments with patients and be certain to inform the small group of patients for whom laparoscopic power morcellation may be an acceptable therapeutic option that their fibroid(s) may contain unexpected cancerous tissue and that laparoscopic power morcellation may spread the cancer, significantly worsening their prognosis.

Capitol Hill

Senate Bill Gives FDA Power Over Hiring, Salaries, & Structure

(Continued from page 1)

The bill, introduced by Sens. Lamar Alexander (R-Tenn.) and Patty Murray (D-Wash.), looks to improve coordination within and between FDA medical product centers and allow the FDA to update its structure, as well as make it easier for the agency to hire; improve access to scientific meetings for federal employees; and streamline processes for NIH research information collection.

"With so many patients and families waiting and hoping for new, safe, effective cures and treatments, we should absolutely work to strengthen hiring practices and break down siloed research that get in the way of innovation," said Murray. "I'm pleased that the committee has reached agreement on legislation to help ensure the FDA and NIH are able to keep the best researchers, doctors and scientists on staff, and to break down barriers that may impede important collaboration. I'm very hopeful that we can continue working in a bipartisan way to agree on strong mandatory investments in the NIH and the FDA as well as policies to strengthen patient and consumer safety—each of which, as Democrats have made clear, are necessary to reach a final agreement."

The bill allows the FDA to conduct a pilot program to test the best ways to boost communication between different centers at the FDA—allowing scientists focused on treatments and cures for a particular disease to better share information, and also exempts NIH research relying on voluntary data collection from the Paperwork Reduction Act, which in this instance is duplicative and slows researchers from moving forward in research, the two senators said in a statement.

"This bipartisan bill takes a significant step to improve FDA and NIH's ability to deliver on the promise of this exciting time in science, by helping them hire and retain top performers and cutting red tape that actually obstructs their ability to keep up with the newest scientific advancements," said Alexander.

Members of the Senate's health committee are scheduled to debate and vote on the bill April 6.

"Senator Alexander and Senator Murray have taken an important and crucial step forward by acknowledging the opportunity and need for innovation at the FDA," said Ellen Sigal, chair and founder of Friends of Cancer Research.

The bill also plans to increase the FDA's ability to retain talent, and pay a salary that is more competitive with the private sector.

"Improvements in human resources management and capability are essential if the FDA is to ensure that safe and effective new medicines, which are being developed with increasingly complex science, reach patients as efficiently and quickly as possible," said Jim Greenwood, president and CEO of the Biotechnology Innovation Organization.

Slamming the Door

Part VIII - A Talk with DePinho

(Continued from page 1)

Recently, I asked Dan Fontaine, MD Anderson's executive chief of staff why the money never changed hands.

"At the time that the consternation and the questions were being raised, things seemed to be going about internal workings at CPRIT that we were not a privy to," he said. "It still became apparent that there was at least one constituency within CPRIT that felt—even though the RFA had specifically said that it was going to go through the commercial review group—that it needed to go through both the commercial review group and the scientific group.

"If the process was going to change to do that, we felt that it was important to be very clear that we were happy to let the process take place a second time and have whatever we had submitted go through both review processes. So we wrote a letter, as you may recall, to CPRIT and we suggested two things: kind of belt-and-suspenders:

"We said that, number one, whatever additional review process you want it to go through, please have it go through. And if there's questions raised; if there's more scientific information that is wanted, since this is supposed to be a business plan—if there's more scientific information that is wanted, we would be happy to supplement that as requested. So we would be happy to do whatever additional review process CPRIT wanted to do at that point in time.

"Secondly, we also suggested that we would even allow CPRIT to hold the money in escrow for a year, to see what kind of milestones we hit with progress on the grant.

"They wrote us back and said we'll put it through the additional review process, thank you very much, and we're not going to make you put it in escrow for a year, because once we've gone through the award process, we will make the award immediately.

"So at that point in time, we anticipated that there would be some sort of additional review process. As it turned out, I think in looking back, other things and other controversies at CPRIT began to arise. To my knowledge, they never put it through an additional process. We never resubmitted, because there was never an RFA or any communication to us.

"I know there were a couple of instances when we may have contacted them and said is there anything else—but, you'll recall, shortly after that the controversy grew to the point that the granting was stopped at some point in time. There were directives, etc. And we never got beyond that point. We never resubmitted; they never re-reviewed. And funds never changed hands."

As all of this was proceeding, Gilman told me that he couldn't understand how the MD Anderson proposal in its original form could get through scientific review. There was nothing there to review.

On the purely aesthetic level, he was surprised to see the word "prosecute" used in the context of clinical trials and discovery program. If you look at the proposal as submitted, it suggests deep, complex research, but calls it commercialization. This wording struck Gilman as particularly perplexing: "CPRIT funding will also provide the resources necessary to strategically invest in innovative chemistry platforms to tap into previously 'undruggable' target classes."

Indeed, the number of academic researchers and pharma companies seeking to do just that is not small. Why should the MD Anderson group be allowed to get funding for this endeavor based on a 211-word paragraph in a six-and-a-half-page document?

Is the following enough information to support a funding decision?

"CPRIT funding will also provide the resources necessary to strategically invest in innovative chemistry platforms to tap into previously 'undruggable' target classes. Current chemotherapeutic agents target a restricted portfolio of protein targets, including kinases and nuclear hormone receptors. The IACS team has developed a work plan to go beyond this limited repertoire of targets by leveraging inhibitors that are

outside classical small molecule physicochemical drug space (including as one example, phosphatases) and leveraging proprietary delivery platforms to bring the therapeutics to the site of action. We plan to execute on our work plan by deploying cross-functional teams of medicinal chemists, pharmacologist and drug metabolism scientists to rapidly advance this proprietary chemistry platform through progressively more challenging hurdles from cell lines, to rodent models, and ultimately to canine and/or non-human primate models in a series of well-defined proof of concept studies. Further opportunities exist through collaborations with investigators such as Dr. Venkitaraman at the University of Cambridge around drugging protein-protein interactions known to be essential for tumor maintenance. By opening up a new druggable space, we believe these platform assets will be optimally advanced through the formation of a Texas-based NewCo and this strategic expansion will provide an opportunity to this entrepreneurial exit at an earlier time point than with other programs."

Most importantly, Gilman wanted to know, how is this not research?

When Fontaine and I spoke recently, he said that as IACS moved forward, it became a commercial success.

"I really think that four years hence, our commitment to bridging that gap between the discoveries in the academic world and products in the commercial world, which is what the [IACS] was designed to do, I think history is on our side on this one," he said.

"I think it's being proven out that we are on the right path. And I'm not sure that Dr. Gilman's resignation had anything to do with that at all, or the resignations of any of the scientific board. We went on without the CPRIT grant, and while I think all of the benefits of the [IACS] are yet to come, certainly there are some early successes in what we have been trying to do, partnered with our strategic industry ventures department, to really put together ways of accelerating discoveries into therapeutics and diagnostics."

Fontaine's words prompted me to request documents under the Texas Public Information Act. Based on preliminary responses, it appears that some information will be released.

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During our first conversation, a few days after Gilman submitted his letter of resignation, he wanted to make sure that I understood the nuanced nature of the story.

The politics of CPRIT was one aspect. The politics of MD Anderson was another. Science policy, regulation of conflicts or interest, the structures of drug development and transfer of technology from academia to the private sector also figured in the story as well.

And that's just for starters.

I assured Gilman that I understood, but made the argument that this is all one massive story. I would jump in and let it develop. Sure, it's a broad as Texas. I would just have to deal with it.

In the summer of 2012, a few months in, I started to realize that I was trying to describe a Texas landscape by looking through a peephole. It was difficult to imagine that just a few months earlier I had no idea who DePinho was. It was all the more scary that I had no deep understanding of IACS and the manner in which it fit into MD Anderson's structure.

So, in the summer of 2012, DePinho and I met at a coffee shop off DuPont Circle, in Washington. He was in town for a meeting at Brookings Institution.

My office is a couple miles away, so I rode a bike down Massachusetts Avenue. There was a tape recorder in my pannier. Also, I had a notebook with a few simple questions. To be fair, I sent the questions to DePinho a few days earlier. The deal was, the conversation would be on record.

As we sat down, DePinho told me about his father's arrival in America as a stowaway, and about his father's cancer, and about the way his father's death shaped his career, moving his focus from science for its own sake to science aimed at producing drugs, saving lives. He told me about Lynda's immigration from China, her adolescence spent above a laundry in New York's Chinatown.

He told me that he fully realized that my coverage wasn't self-serving, that I am interested in the public good.

I assured him that this was correct, and that I was finding it a bit unsettling to be in anything but a friendly relationship with MD Anderson. I told him that, like Alvaro DePinho, I am an immigrant, though not a stowaway. I came here from the USSR at age 14, in 1973. During his first year in the US, my father, a writer and poet, pushed a broom.

I don't hide my immigrant roots. My kids, friends and colleagues are well aware of them, but my immigrant roots were not a part of the story I was supposed to cover at that coffee shop. And it's certainly not unusual for an immigrant kid to do reasonably well in this country.

Then I went on to disclose something even less relevant. I said that when my mother was diagnosed with ovarian cancer, she received Taxol, then a new drug, in a clinical trial at NCI. After Taxol failed, she went to MD Anderson.

Though my mother died of her disease, going through a thorough evaluation of available options by MD Anderson physicians proved to be an extremely valuable experience for my father. It gave him the assurance that everything that was available was, in fact, tried.

The doctor who treated my mother is a fantastic, compassionate man, Andrzej Kudelka. He is the sort of doc who gave his patients his home phone number and his direct number that bypasses the receptionist. When I run into him, which happens roughly once a year, he asks me how my father is doing.

All of this is, of course, true, but by opening my mouth, I made my mother a part of the story.

It was as though cancer suddenly became a personal attack. It is not. It's a molecular process devoid of capability to discern whether its host is Alvaro DePinho of Sofia Aronovna Goldberg.

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That morning, DePinho and I didn't get around to doing the Q&A. There was too much other material he wanted to cover, and the noise from city buses made it impossible to tape. We decided to try again—over the phone.

A few days later, he took my call. I told him that I would have my tape recorder running.

For months, DePinho was receiving a massive amount of attention from The Cancer Letter, far more than Harold Varmus, director of the National Cancer Institute. If I can be forgiven for lapsing into the war metaphor, if DePinho is a general in the war on cancer, Varmus was the field marshal, perhaps even generalissimo.

It was possible that I was unfair in devoting so much attention on DePinho's every move. He was owed an opportunity to explain himself in a way that was completely unfiltered.

To his credit, DePinho didn't avoid me. Our on-record conversation clearly lays out the DePinho story as he saw it at the time. Originally published Sept. 7, 2012, it remains an important document.

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PG: *In your job interviews, originally with the UT System chancellor and the regents, you were asked, I'm sure, to describe your vision for MD Anderson. In a nutshell, what were the plans you described for them?*

RD: The interview process was a very essential and lengthy one, during which I was asked to describe my vision for MD Anderson and for cancer care in the future, which, I'm sure, was asked of all the candidates.

PG: *Of course. What was your answer?*

RD: If I recall, just to distill it down to the most elemental points, the major emphasis was that we were entering into an era of science-driven cancer care, in which patients would be administered therapies that would be more effective, based on their genetics, and also avoiding toxicities based on their inherent genetic make-up.

That was an important aspect that permeated most of my comments. I also spoke about the need for increased prevention and early detection.

Prevention is one area that really focuses on understanding why we get cancer in the first place, also developing the right educational tools that enable us to, for example, protect children from sun exposure, to reduce childhood obesity as well as to prevent children each and every day from starting smoking; things of that nature.

Also with respect to early detection, this is where I think some of the greatest near-term impact is going to occur, with the revolution ongoing in serum proteomics and imaging. We have a tremendous opportunity to shift our discovery of cancers to much earlier stages, when the chance for cure is greater.

I place a great deal of emphasis on prevention and early detection.

PG: *Would this be what you were going to do at MD Anderson—look at prevention and early detection?*

RD: I think in general, the field of cancer has focused significantly on understanding the genetic basis of cancer and focusing significantly on treatment, which is continuing to be a major emphasis for us. But I mentioned that we are entering into an era where we can be far more proactive in understanding cancer genesis and using that knowledge to prevent disease—look at the revolution that occurred as a result of the HPV vaccine, the knowledge of hepatitis virus, H. pylori.

These are all opportunities for us to understand what drives cancer and intervene in ways that are most effective. I think that the future, while it will continue to focus heavily upon the treatment of advanced disease, will also focus increasingly on preventive-interventive

strategies as well as early detection.

PG: *So that's your vision for MD Anderson?*

RD: Actually, this has been part of our mission for some time. I think it's a matter of emphasis, but it has been central to our mission for many, many years.

PG: *Did you get to mention the biotech incubator at that point, or was that not a large enough…*

RD: Not yet. But just to finish your first question, the other thing that I also expressed strong interest in, during the interview, was the maintenance of academic excellence.

I talked a lot about mentorship, enhancing our trainee experience, enhancing the ability of our junior faculty to develop sustainable careers, making sure that physician scientists, who wear many hats, are fully supported to achieve the kinds of translational activities that are critically important to drive discoveries into practical endpoints that make a difference for patients.

Your next question?

PG: *Was the incubator part of the plans you discussed then?*

RD: No, but perhaps you mean the Institute for Applied Cancer Science?

PG: *Correct.*

RD: If you are talking about the Institute for Applied Cancer Science, Giulio Draetta is the director—he was Merck's worldwide head of oncology drug discovery, and prior to that vice president of Pharmacia. The IACS is based on the construct of an institute that started 2003 at Dana Farber called the Belfer Institute for Applied Cancer Science, an institute that focuses on trying to drive discoveries to drug-development endpoints.

It's a new organizational construct that's designed to rigorously validate targets, develop drugs against those targets, and develop a clinical path hypothesis, so that we can test these novel drugs in the right patient population.

We had some success in Boston, and I was eager to explore similar possibilities on the scale that MD Anderson could provide.

PG: *So it's a way of making it bigger?*

RD: Not necessarily bigger, but we added some very exciting components to it that in the area of biotherapeutics, whereas in Boston, we were focused mostly on small molecules, so we've expanded into a number of areas.

So the institute supports professional staff that are focused on timelines, deliverables, and milestones, who work in collaboration with the academic investigators, and together move knowledge forward in a very directed way toward drug development endpoints that make a difference for patients.

PG: *And so what were the promises that the UT chancellor and the regents made to you, what mandate did they offer?*

RD: If you're talking about CPRIT, there were no promises because CPRIT is an independent state agency over which UT System has no control.

PG: *Well, I guess what I'm really wondering about is did the CPRIT funds figure into it in any way at all?*

RD: I see what the confusion is, because you are going back between UT System and CPRIT.

PG: *Correct. I'm not necessarily confused; I mean, I understand the difference…*

RD: Because you don't know.

PG: *I don't know.*

RD: So the Institute for Applied Cancer Science was a construct that we had at Harvard that we wanted to recreate at MD Anderson. That had nothing to do with CPRIT, it was something that was focused on what MD Anderson should do, and that was a discussion that occurred with [UT Executive Vice Chancellor for Health Affairs] Ken Shine and the Board of Regents as a means of bringing individuals down like Giulio Draetta, Lynda Chin [Department of Genomic Medicine chair and IACS scientific director], Phil Jones [head of drug discovery] and others to basically have that same construct be developed at MD Anderson.

So that was a discussion that occurred with the regents, MD Anderson and numerous individuals. I wasn't involved in the Institute for Applied Cancer Science—that wasn't one of the things that I was discussing with the regents or with Ken Shine.

PG: *You did not? I thought that would be a crucial part of what you would do? Or…?*

RD: Lynda Chin, Giulio Draetta—they are independent investigators. And in recruiting them down, that discussion was focused on them: where they would have the opportunity to develop their programs that they had in Boston and transplant their activities to MD Anderson.

PG: *So that was occurring subsequently to your being offered the job?*

RD: Some conversations were simultaneous and some were subsequent. They were all part of the negotiations to try to bring the entire group of individuals down.

PG: *I see. So these were different negotiations within the whole process?*

RD: They were the typical negotiations that

tend to occur between academic investigators and institutions. There is nothing different that was any different from, let's say, us recruiting investigators recently like Sam Hanash, who is now leading a very important proteomics early detection program here, or any different from our recruitment of Jim Allison, where we've invested significantly into our immunology program, or any different from Raghu Kalluri, who is coming down to head our program of cancer biology, or any different from Andy Futreal [professor of genomic medicine], where we made very significant investments in genomic medicine.

PG: *When did Dr. Chin's incubator proposal emerge?*

RD: Now you're talking about the CPRIT side of the equation.

PG: *Right.*

RD: Let me put this into a bit of a context. When we came down early on in September, October—Giulio, Lynda, myself, Phil Jones, Eric Devroe [executive director of strategic alliances]—there was great community interest in Houston in trying to understand the Belfer Institute.

There was also great interest in starting biotechnology industry in Houston, and so many individuals asked us to talk about matters of translation, commercialization, and some of these novel constructs.

During the course of those months, there were numerous presentations that were made—I must have made personally at least three or four in which we had many components of the Houston community listening to our presentations.

PG: *When was Dr. Chin's incubator merged with rest of the…*

RD: I'm leading to that. At that point, there were individuals who came to us from CPRIT that were extremely interested in what we were talking about and recognized a proposal that had been submitted to CPRIT by Rice as an incubator. Rice had an excellent infrastructure; they had a very good proposal, but they didn't have content for that incubator—something that we generate through the IACS—the content to incubate assets for ultimate commercialization.

And so, the idea was proposed by CPRIT that we should join forces with Rice. I believe those discussions occurred in late November, early December. We were then alerted to the fact that there was this request for proposals in the incubator commercialization group for a component of CPRIT.

The leadership of the institute—which was Guilio Draetta, Lynda Chin, Eric Devroe and Phil Jones—got together with the Rice colleagues, and, under the guidance of the commercialization team at CPRIT, organized this cohesive entity. And that took about two to three months of planning and back and forth, all under the guidance of CPRIT.

PG: *I've seen that e-mail from CPRIT, which I got under the Texas freedom of information law, and it appears that that Charles Tate, who's a member of CPRIT oversight committee and commercialization board, is being mentioned as playing a role in devising the application. What role did he play in this process?*

RD: I think that that's a question you need to ask CPRIT. I don't know. My understanding is that he is involved on the commercialization side of things, but to my understanding, I do not know of any role that he played, but I would ask that you ask CPRIT or ask Charles Tate himself.

PG: *I will, of course. But there were no conversations between you and him?*

RD: No one even knew about the institute until we started talking about it after we were here on the ground at Texas and then months after that, this request for consideration that we would merge with Rice emerged. And then we went through the process under the guidance of CPRIT to eventually file the grant.

PG: *Does the governor's office plays a role, or lieutenant governor, or the legislature in what you are trying to accomplish in MD Anderson?*

RD: No direct role as it relates to our CPRIT funding, but because MD Anderson is a state institution, we do receive crucial funding from the state of Texas to eliminate cancer, which is what we're trying to accomplish at MD Anderson. The governor did visit MD Anderson to celebrate the opening of the Institute for Applied Cancer Science early on. There was a major press conference for that, but none of the individuals were involved in any way with the incubator proposal.

The Institute for Applied Cancer Science staff submitted a document that was requested in the Request for Applications, and that is what occurred.

PG: *The MD Anderson proposal for the incubator is less than seven pages long, and it was funded to receive $18 million three weeks later. It's sort of unusual, did that in any way surprise you that it was so quick and so successful?*

RD: I wasn't involved in the detailed aspects of timing and things of that nature.

As the chancellor's external report reviewed, there was a very specific timeline of activities that occurred.

The grant was submitted, it was reviewed by an

external review team from outside the state and then the recommendation went to the oversight committee and it was recommended for funding.

With respect to the length of the proposal, my understanding is that CPRIT gave very clear guidance on the nature of the proposal and what was to be in the proposal. Second, the point about it being a lot of support—as you know, cancer drug development is extremely expensive—you might know that it takes on average between $15 and $40 million dollars in industry for a single Investigational New Drug, on

average, collectively per IND about 140 FTEs [full-time equivalents].

So the drug discovery and development process is very expensive if you are trying to develop lead clinical candidates as opposed to research tool compounds.

PG: *Since you have withdrawn this proposal and you are now resubmitting the document, what would it look like, and will you be resubmitting it for scientific review as opposed to just commercialization?*

RD: First, I'm sure it's going to be a very, very strong and compelling proposal—the progress in the institute has been quite impressive.

Although we didn't withdraw the original document, we did offer to resubmit and will do so. We are waiting for the revised commercialization request for proposals now and I'm confident that the IACS leadership will respond fully and creatively with a proposal that demonstrates the expertise, the intellect and resources that we have at the institute.

PG: *So it will be longer than seven pages this time around.*

RD: I actually don't know. I think we're waiting for the guidance from CPRIT, but I'm not involved at that level.

PG: *Will it go through a scientific review as well, or…?*

RD: My understanding is that there are going to be commercialization and scientific review. You may want to check with CPRIT.

PG: *I will.*

RD: I think it would be an extremely welcome and healthy way of reviewing the grant, but I'm not familiar with the guidelines at this point or what the content of the grant would be.

PG: *Well, let's just be done with the incubator, but I guess the more interesting question is, what role does the institute play, within MD Anderson structure? And what role does Dr. Chin's scientific vision play at MD Anderson now?*

RD: First of all, Dr. Chin plays a very important role, just as all of our department chairs do. She is chair of a new department of genomic medicine, and her focus is on genomics at a precise moment when technology and scientific thought, concepts, are coming together to cause major disruptive change in the way that cancer is viewed and treated.

She'll sink or swim on her own scientific merit and accomplishment here. I have great confidence in her ability to succeed, as evidenced by her track record, her stature in the field and her publications, including her recent Cell paper that just came out.

In the institute, she is the scientific director and she is one of the leadership group under Giulio Draetta, along with Phil Jones, Jannik Andersen [senior associate director of drug discovery], Joe Marszalek [senior associate director of target validation] and others that are in the leadership group that help manage the myriad activities that occur in the institute.

PG: *It must be really challenging to work closely with one's spouse. How is that working out for you?*

RD: We have always been bound together by our common interests, not just in our family lives, but in our scientific lives and it's been a tremendous source of, what's the right word…Well, it has just been a very gratifying experience to share a common passion.

So, we have always been able to work very effectively together, because while we work in the same area, we emphasize different things. I'm more of a cancer biologist and geneticist, whereas Lynda is more focused on genomics. And I also work on aging and she doesn't work in that area.

PG: *At this point, it's just a potential for, basically, side conversations—and just the difficulty of managing the potential conflicts and appearances of conflicts.*

RD: Anybody that's in the room for a few minutes with each of us recognizes that we actually spend very little time talking about science.

With three young children, we tend to focus most of our energies on raising our kids whenever we do have time together. We had, over the years, joint lab meetings—that's where most of the professional interaction is.

Just to give you an example of how little we do communicate on the scientific level, it came as a surprise (to me) that Lynda had a paper published in Cell. And the way I found out about it is that MD Anderson had a press release today and I read the press release and I saw Lynda's name in it and I'm reading on it, and I thought maybe she was commenting on another group's paper, and it turns out that it was her

paper in Cell.

So we are independent, we are colleagues, and we do have a lot of common interests scientifically—but we don't spend a lot of free time together on our jobs. In the time that we do spend together, we tend to focus on family, our children and each other.

PG: *I understand that you've said in the past that you made a financial sacrifice to come to MD Anderson, is that correct?*

RD: I have never said that I have made a financial sacrifice. I have said that I've made a sacrifice or a personal sacrifice and I feel very honored and privileged to be the leader of MD Anderson, an extraordinary institution that each and every day does amazing things for many, many thousands of patients here and around the world.

PG: *What was the sacrifice?*

RD: To put it in perspective, Lynda and I spent four years renovating our dream home in Brookline, Massachusetts, and we were a few months away from completion, when the call came to lead this great institution. We felt that the choice, really…that that option took precedent over any personal challenges that we might have.

Also, our three young children were happy in school with their friends, they were thriving, and Lynda's career was going very well. We had a very large support network of both of our families and relatively near in New York City. Dismantling all of that, particularly uprooting our children, was not easy but leading an institution such as MD Anderson is a tremendous honor and we're delighted with the career choices we've made.

We've had the most fulfilling year of our lives, the children are amazingly adaptive, the schools in Houston are extraordinary, the arts wonderful. The quality of life here is spectacular.

It's a vibrant city with great culture; great personality, and we feel very welcomed in Houston and it's been a very, very gratifying experience overall. And I feel blessed, and I guess that's all I have to say about on that matter.

PG: *What were some of the business interests which you have that—investments and equity stakes in companies—that you had to give up or sell? How were those decisions made, about what stays and what goes?*

RD: Sure. I have made a complete disclosure to the UT System and also to the Texas Ethics Commission, so you are free to look at that public information if there's anything specific.

But on a high level, I eliminated my role in a number of companies that I was advising them in, due to the limitations of time and the need for intensive focus in the job that I now have the privilege of having.

The only companies that I elected to remain on were companies that I felt I was playing a special role that was essential for the success of the company, and by extension, where my role would help the companies succeed so that they could help patients.

The three companies were AVEO Pharmaceuticals, which is a company that Lynda and I co-founded over ten years ago. It's focused on the development of drugs using sophisticated genetics and cancer biology as well as mouse model systems. The other one was Metamark Genetics.

Again, we were co-founders of that company and that company is focused on diagnostics to develop diagnostics for individuals with prostate cancer, to identify which men are at risk for the development of lethal disease in that context as well as in other cancers such as melanoma.

The third is another company that I cofounded, Karyopharm Therapeutics, which is focused on targeting nuclear export machinery as a novel therapeutic approach for cancer.

PG: *And you got rid of?*

RD: Again, the complete list of a few companies should be in the released documents, but to name a few, I eliminated my role as an advisor for GSK, for Epizyme, for Agios, for Enzon, amongst others, although I still have some equity from my service in Agios and Enzyme.

PG: *And the reason is that they could do well without you, they didn't need…*

RD: That's right. I was not a founder of those companies. I was merely playing a role as an advisor, and the question that I ask myself with anything that I eliminate or retain is, would it impact adversely on the ability of those companies to impact human health.

PG: *So it was basically your own decisions, I suppose, with no feedback from the UT System?*

RD: That's correct.

PG: *You were able to make the proposals—this is how you're going to deal with the conflicts and they said, fine?*

RD: Yes. And they have very strong conflict management procedures that are in place and we could give those procedures to you.

PG: *I would love to see them. Recently there was some press coverage of AVEO trial that was proposed for MD Anderson [http://www.chron.com/news/houston-texas/article/M-D-Andersoninvolved-*

in-trial-of-drug-marketed-3711441.php].

Do you think, in retrospect, that it would have been better not to go forward with that study, which of course required you to seek a waiver for it to continue? Are you still seeking a waiver?

RD: First of all, there has been a recent story in the press and we've been successful in correcting some of the misinformation in that story.

We have not gone forward with the proposed AVEO study and it will not go forward until we receive guidance from UT System on the conflict issues.

Also, no waiver has been requested with respect to this specific proposed AVEO study. A general waiver of certain provisions of MD Anderson's Conflict of Interest Policies as they pertained to a number of companies, including AVEO, was submitted to UT System.

Hand-in-hand with the waiver request was a detailed proposed plan to monitor and manage conflicts of interest if the waivers were granted.

Shortly after we became aware that AVEO issued a news release incorrectly implying that the study was open at MD Anderson and that a member of MD Anderson's faculty was the lead investigator, we asked AVEO to clarify the release, as it would not be possible for the lead Principal Investigator to be at MD Anderson even if UT System granted the pending waiver, because of other rules that we have that manage conflicts of interest. It's important to understand that those discussions between AVEO and MD Anderson started, I believe, in 2009.

This was a number of years before the job for MD Anderson president even emerged. But at this point, the trial will not open at MD Anderson unless the waiver is approved by UT System.

PG: *So you're still seeking the waiver?*

RD: Yes. Absent a waiver, AVEO is unable to sponsor any research if the principal investigator is at MD Anderson.

PG: *Right. With waiver requests, or one single waiver?*

RD: One single request has been sent to UT System, but it includes multiple waiver requests and is not exclusive to this trial or to AVEO, and it includes a comprehensive conflict management plan depending on the company and type of trial involved. For instance, there are different rules depending upon whether the trial involves patients or not.

PG: *Are you still aiming for the goal you called the moon shot? And does it still mean curing five cancers in five years, and is it sort of clear which of the cancers will be chosen, and when will this be rolled out?*

RD: Well, I don't know where you got the "cure in five years" information from, we are…

PG: *I think it was from one of your speeches. If it has changed, that's fine.*

RD: No, no it hasn't changed ever. I think it would be rather unrealistic that we would be able to cure cancer in five years.

PG: *Or five diseases.*

RD: So that we are extremely clear on that one point.

What I have said is that we have reached a point where there is a confluence of technological advances and significant conceptual breakthroughs and clinical proof of concept, such has harnessing the power of the immune system, affecting cell cycle, altering apoptotic responses, and a variety of other hallmarks for cancer where we have drugs that target those hallmarks result in clinical responses, some of which are quite dramatic, that puts us in a position to say that if we organize ourselves in a comprehensive way, in an integrated way, from prevention to early detection to prognostication to treatment and survivorship and recurrence, that we can significantly reduce mortality in this decade for certain cancers.

There are some cancers where we're showing very impressive progress that if we apply what we already know today in a way that is translated and reduced to practice to help patients; in the area of early detection, for example, or in the area of combining very potent drugs with very significant clinical responses, that we will dramatically reduce mortality in those cancers. I can give you a specific example or two, if you'd like.

PG: *I'd love to hear which cancers you are targeting.*

RD: We're actually going to have a review process from an internal and external advisory group, in fact, tomorrow and the next day, and that will allow us to prioritize these cancers.

We'll initially select up to five cancers, inaugural programs, that we feel that we can put a team on the field that the knowledge in that particular area which is positioned for significant progress—diseases where we have great model systems, enough genomic information, drug interventions where we have significant responses in a proportion of patients that we can build on these current successes and make significant advances.

So based on those guiding principles, we will

have selected inaugural programs, but the exercise of going through this strategic planning has set the stage for ultimate cure in the decades ahead, that what we are focused on is trying to develop a strategy for all of the major cancers that we're focused on here, and for those that are not selected, this process will have identified areas for strategic investment at MD Anderson and our collaborators around the country and around the world to work together towards organizing this significant effort that leads to impact on patient survival.

PG: *So what's the target of when this will happen and which cancers…?*

RD: We will make an announcement in September around the 50th anniversary of Kennedy's moon shot speech which occurred here in Houston in 1962 and it's an aspirational effort that, I think, is quite realistic based on the technological advances and based on the tremendous progress that we've made in the field in a number of cancers.

PG: *What's the target date to have these cancers, if not eliminated, controlled?*

RD: I think it would be very difficult to answer that question. I think nobody knows the answer.

PG: *You do not have that date?*

RD: No, of course not, I think it's just not possible to know that. But I do think, and I'm sure you would agree, that we've reached a significant turning point in history of the field. Let's take melanomas, for example.

In melanoma, if one applies across a broad front, strategies and prevention, detection, and treatment advances, we believe that we can make significant reductions in mortality. In the area of prevention, we now know that excessive sun exposure during childhood leads to a dramatic increase in the incidence of melanoma in your 30s and 40s.

So one effort would be to implement educational programs in our schools in much the same we did for traffic safety with seatbelts, and ensure that children and their parents learn that they need to be protected from the sun at that vulnerable period in their lives.

PG: *But that's something that people knew for a long time, and do you need MD Anderson to tell you that?*

RD: The educational programs that exist in this country are highly fragmented and of course, we'll work with the entire system but what we want to do is inspire our schools to have that as part of their curriculum and to organize the information needed—the public service announcements and the educational materials so that we can move forward on that front.

MD Anderson does happen to be the most significant distributor of educational material to oncologists in the world and we would continue that effort in this particular context.

And here I'm giving you just a very specific example. In the area of prevention you would really focus on ensuring that there's good sun protection at a very early stage in life.

Secondly, with respect to early detection, we know from a pilot screening program in Germany that a seven-year screening effort resulted in a 50 percent reduction in mortality, because you are catching these cancers at an earlier stage where the chance for survival is much greater simply by surgical excision.

With regard to early detection, there are also major advances in optical imaging, recognition software that is being developed as we speak to enable us to more rapidly identify skin lesions that would allow us to move forward on, and much improve early detection efforts.

There are also major diagnostic advances in early-stage cancer in melanoma that enable stratification of cancers that are hardwired to progress to lethal metastatic disease. Such prognostic determinants are being developed that allow us to stratify patients into aggressive versus more benign treatment paradigms.

And then, lastly, in the area of therapeutics.

The year 2009 brought truly historic advances on the treatment level, and here the discovery of the BRAF mutation in 2002 from Michael Stratton and Andy Futreal, who's now at MD Anderson, and the development of the drugs squarely directed against that signature mutational lesion has led to a very significant increase in the survival of patients that have that specific event.

In addition, a truly historic event occurred from the work of Jim Allison, also another recent faculty member, who discovered why the immune system is dampened in the context of cancer.

As you know, cancers are not recognized well by the immune system—they appear to be sequestered from the immune response—he discovered a molecule, CTLA-4, that puts the brakes on the immune system, developed the drug against that (anti-CTLA antibody), and now it appears that one in four patients are alive at five years as a result of that treatment.

So let's say we pick melanoma as an inaugural program—we haven't made this decision yet—we would organize our efforts across the broad front involving aggressive educational programs with our school systems, new imaging modalities that

more accurately identify early-stage lesions and new prognostic determinants to identify which lesions are hardwired for lethal progression and finally build on the tremendous therapeutic successes since 2009, with BRAF inhibitors, with anti-CTLA antibodies, some of the newer immune modulating drugs like PD-1 which are showing very exciting results in early trials.

With all of those integrated efforts—it's easy to imagine that the now 25 percent survival rates of advanced melanoma and the impact of the mortality that we now have could easily rise to 50 percent within this decade as a result of those comprehensive activities that apply existing knowledge.

PG: *Does CPRIT have a role in this?*

RD: Well, CPRIT certainly would have a role from the standpoint that part of the way that we're going to be funding this is through a combination of philanthropy as well as through grants from foundations as well as through a number of other federal grants.

PG: *I understand that you have told the clinical department chairs at MD Anderson that they would have to boost revenues by another 10 percent. Is that correct?*

RD: Yes. The clinical divisions have been asked, as in recent years, for an activity of volume increase ranging from five to 10 percent.

But this is for a division as a whole. We have more faculty each year to accommodate these volume increases, so the number of new patients seen by any individual faculty will be no higher than what's achieved in many previous years.

We do target a modest increase of two to three percent in patients seen per provider as we seek to become more efficient over time and enhance, for example, IT capabilities, etc. And we always adjust the number of new patients expected to be seen by the faculty members' stated clinical commitment.

PG: *Will you increase the percentage of salary and grants to basic scientists? I think it was 30 percent and I believe it's going up to 40?*

RD: In 2006, John Mendelsohn [professor of experimental therapeutics and immediate past president of MD Anderson] and Margaret Kripke [professor of immunology emerita and former executive vice president and chief academic officer of MD Anderson] had an external group review of our research. One of their recommendations of the Washington Advisory Group was to increase the salary on grants, which at 30 percent, was significantly lower than comparable institutions.

That was increased to 40 percent in 2011.

Investigators were given about two years advance notice. I wouldn't rule out further increase, but let's remember, at many places, it is north of 80 percent, so this is something we'll evaluate over time.

We also have an incentive plan, and if someone garners more than 40 percent, they get resources back—I believe it is still a very generous arrangement and it helps us both with retention and recruitment.

PG: *I hear some of your staff tell me that there's a great deal of excitement at MD Anderson, but directors of other centers and cancer hospitals are telling me that they are recruiting aggressively on the clinical side at MD Anderson and some are successful. Does this worry you?*

RD: I believe that we have the most outstanding clinical staff that has been assembled anywhere. It has not been surprising that we do lose some wonderful people to other fine institutions so that they can lead other great institutions, but the number recruited away is small when you consider the critical mass of expertise assembled here.

We have 19,000 employees. Nonetheless, we fight hard to keep as many who are offered elsewhere.

We do our fair share recruiting as well and this has been an extraordinary year in recruitment. And so that's more or less what I have to say about that.

PG: *I guess you've stepped on some toes this year and you have stepped on a few landmines as well. What do you think are your strengths and weaknesses as a manager of such a massive institution?*

RD: I'm having the time of my life. I'm new at this job and I believe I'm learning and growing every day and I suspect I'll continue to learn and grow for the next decade or so.

I think I'm open and direct and I try to be respectful of everyone I work with. I probably try and pack quite a bit into each day—perhaps too much, but I also want to see my children for breakfast when I can.

John Mendelsohn and both his predecessors were all amazingly successful during their tenures as president, and that's the great strength of MD Anderson.

PG: *What about your strengths and weaknesses as a manager?*

RD: Well, we now are, once again, ranked number one as the best cancer hospital. We have had our most successful year financially in its history. We have successfully recruited a number of extraordinary faculty and administrators. We are number one in NCI grants; we're competing very effectively.

The largest number of high-profile papers in the

history of the institution—Cell, Science, Nature, New England Journal of Medicine, and other journals of note—I think that we're doing well as reflected by the progress that we've made in the institution.

PG: *Was there a humbling moment—I have one every week, on a good week. Was there anything that you wish you had done differently?*

RD: I think that a greater level of communication with respect to how the CPRIT episode was handled—would it have been better perhaps if they'd been more proactive to really explain what occurred factually. We attempted to do that again with respect to this recent story on AVEO, but unfortunately the facts were not as, let's say, incorporated into the story.

So I think finding ways to be more effective in communicating across many different constituents in such a large and complex organization is something that I need to strive and work for each and every day.

PG: *Well, thank you very much.*

Bunn Wins ASCO Karnofsky Award; Kaelin to Receive Science of Oncology Award

The American Society of Clinical Oncology announced the winners of its highest honors, the Special Awards, to be presented during the 2016 ASCO Annual Meeting in June.

"The exceptional accomplishments of each of our awardees reflect their exemplary dedication to furthering cancer research and serving as a beacon of hope to the cancer community," said Peter Paul Yu, immediate past president of ASCO and chair of the Special Awards Selection Committee. "It is our honor to recognize their enduring contributions with ASCO's most prestigious awards."

The 2016 Special Awards Honorees are:

Paul Bunn Jr., the David A. Karnofsky Memorial Award and Lecture.

Bunn is a distinguished professor of medicine and the James Dudley Endowed Professor of Lung Cancer at the University of Colorado School of Medicine. He is the principal investigator of the SPORE in Lung Cancer grant at the University of Colorado. Bunn's work focuses on identifying novel diagnostics and treatment strategies for lung cancer.

William Kaelin, the Science of Oncology Award and Lecture.

Kaelin is a professor of medicine at the Dana-Farber Cancer Institute and Harvard Medical School, and a senior physician at Brigham and Women's Hospital. His research focuses on understanding how mutations in tumor-suppressor genes affect cancer development. His work on the VHL protein was instrumental for the subsequent successful development of VEGF inhibitors to treat kidney cancer.

Ethan Dmitrovsky, the ASCO-American Cancer Society Award and Lecture.

Dmitrovsky is the provost and executive vice president of MD Anderson Cancer Center. He is being recognized for his groundbreaking work in retinoid differentiation therapy for acute promyelocytic leukemia.

Pierre Soubeyran, the B.J. Kennedy Award and Lecture for Scientific Excellence in Geriatric Oncology.

From designing trials for non-Hodgkin lymphoma to implementing screening methods, Soubeyran has focused on the care of older patients in the U.S. and in his home country of France. His work has been critical to the development of geriatric oncology at both the clinical and research levels.

David Johnson, the Distinguished Achievement Award.

Johnson is chairman of the Department of Internal Medicine at The University of Texas Southwestern Medical Center, and is being recognized for his decades-long career in internal medicine and oncology, and his mentorship of physicians at UT.

Philip Hoffman, the Excellence in Teaching Award.

Hoffman is a professor of medicine in the Section of Hematology/Oncology at the University of Chicago's Pritzker School of Medicine. He was one of the original Masters of the Academy of Distinguished Medical Educators at Pritzker and has been honored as a favorite faculty member 25 times by graduating medical students.

C. Kent Osborne, the Gianni Bonadonna Breast Cancer Award and Lecture.

Osborne is a professor of medicine and molecular and cellular biology and the director of the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine. His research on hormone pathways involved in breast cancer has been instrumental in identifying fulvestrant as a potent endocrine therapy. His pioneering research on the mechanisms of resistance to targeted endocrine therapies has affected the lives of many patients with breast cancer.

Quyen Chu, the Humanitarian Award.

Chu is chief of surgical oncology and the Charles Knight Sr. Endowed Professor of Surgery at Louisiana State University Health Sciences Center in Shreveport. Chu has traveled to countries such as Vietnam, Iraq and Nicaragua in hopes of improving cancer care for patients in low-income countries.

Susan Braun, the Partners in Progress Award.

Braun is CEO of The V Foundation for Cancer Research. She is being recognized for her service in leadership roles at several major cancer nonprofit organizations throughout the past 20 years.

Susan Cohn, the Pediatric Oncology Award and Lecture.

Cohn is a pediatric oncologist at The University of Chicago who specializes in patients with neuroblastoma. She is being recognized for her leadership in the development of a series of risk-based clinical trials to improve treatment for low- and intermediate-risk neuroblastoma and survival for high-risk patients.

Waun Ki Hong, the Special Recognition Award.

Hong's expertise spans more than 36 years of translational and clinical research, and he has been an advocate for chemoprevention of epithelial cancers and emphasizing the importance of personalized cancer therapy. His recent achievements include the development of biopsy-mandated, targeted therapies for lung cancer based on genetic abnormalities in tumor tissue.

The Fellow of the American Society of Clinical Oncology distinction recognizes ASCO members for their extraordinary volunteer service, dedication, and commitment to ASCO. Their efforts benefit ASCO, the specialty of oncology, and, most importantly, patients with cancer. The 2016 recipients of this distinction are:

- Ethan Basch
- Susan Cohn
- Mary Disis
- Gini Fleming
- Jennifer Griggs
- Dawn Hershman
- Clifford Hudis
- Joseph Jacobson
- Rogerio Lilenbaum
- David Spriggs
- Alan Venook
- Victor Vogel
- Sandra Wong

ASCO acknowledged the support of the American Cancer Society for the ASCO-American Cancer Society Award and Lecture; the Alliance for Academic Internal Medicine and The John A. Hartford Foundation for the B.J. Kennedy Award and Lecture for Scientific Excellence in Geriatric Oncology; and GlaxoSmithKline Oncology for the Gianni Bonadonna Breast Cancer Award and Lecture.

Obituaries

UNMC's Glenn Dalrymple, 81

Glenn Dalrymple, a radiology professor at the University of Nebraska Medical Center from 1990 to 1996, died March 9 in Omaha after a long battle with colon cancer. He was 81.

A native of Little Rock, Ark., Dalrymple spent the early part of his career in Little Rock, spending 16 years on the faculty of the University of Arkansas for Medical Sciences, 11 years in a private practice radiology program, and two years with the John L. McClellan Memorial Veterans Administration Hospital.

He joined UNMC in 1990 as professor of radiology and internal medicine and played an active role in UNMC's cancer research program. One of his areas of expertise was nuclear medicine, a medical specialty involving the application of radioactive substances in the diagnosis and treatment of disease.

He also served as interim chair of the UNMC Department of Radiation Oncology (1993-94) and as interim chair of the department (1994-96). He retired in 1996.

Dalrymple was a captain in the U.S. Air Force, serving as director of the Space Radiation Effects Group, Radiobiology Branch in the School of Aerospace Medicine at Brooks Air Force Base in Texas. His team estimated the radiation risks to astronauts in the early years of the space program.

"He was a man of spectacular intellect, genuine kindness and a deep appreciation for medicine and education," said Charles Morris, professor of radiology at UNMC. "He was a superb clinician, a prolific researcher in both clinical radiology and radiation biology, and a wonderful teacher."

Dalrymple had a lifelong commitment to symphonic music. He and his wife of 61 years, Mary Jo, were founders of the Arkansas Symphony Orchestra, and Dalrymple played the French horn and trombone with the ASO for 35 years.

Upon moving to Omaha, the Dalrymples again founded a community symphony. Dalrymple played with Orchestra Omaha for 15 years, including several years with the additional challenge of low vision.

"I considered Dr. Dalrymple to be my greatest mentor and teacher, and most of all, a great friend,"

said Nina Baranowska-Kortylewicz, UNMC professor of radiation oncology. "Glenn was a true Renaissance man. He was always an avant-garde when it came to music—he loved Gustav Mahler. He was an innovative photographer, and he left a wonderful legacy for UNMC Radiation Safety by bestowing several of his photographs to the department."

Dalrymple is survived by his wife, Mary Jo, and children Anne Dalrymple (John Keenan) of Seattle, and Mark Dalrymple (Sharlotte DeVere) of Pittsburgh. He also is survived by one grandchild, Zoe Keenan, of Seattle.

Memorials should be made to the Weigel Williamson Center for Visual Rehabilitation at UNMC, the Nebraska Humane Society, Orchestra Omaha or The Intergeneration Orchestra of Omaha.

MSKCC's Robert Golbey, 93

Robert Golbey, who spent 35 years at Memorial Sloan Kettering Cancer Center, died at his home March 12, with his wife, Monica Hunt, and son, Seth, beside him. He was 93.

After joining MSKCC in 1955, Golbey helped establish and lead the Solid Tumor Service, and implemented studies for the treatment of testicular cancer. Golbey was born in Brooklyn in 1922, and received his medical degree at New York University.

In addition to his medical career, he achieved the rank of brigadier general in the U.S. Army Reserves, and served in the Korean War.

Golbey requested that any remembrances be made in his memory to The Landings Military Relief Fund for Families, or to Hospice Savannah.

In Brief

Yanai to Lead New Institute For Computational Medicine At NYU Langone Medical Center

ITAI YANAI was named the inaugural director of the Institute for Computational Medicine at **NYU Langone Medical Center**, effective May 1.

The Institute for Computational Medicine will act as the hub for multidisciplinary efforts to reveal patterns in medical data to aid in diagnoses and the design of new treatments.

Yanai will also hold the academic title of professor in the Department of Biochemistry and Molecular Pharmacology at NYU School of Medicine. He comes to NYU Langone from the Technion-Israel Institute of Technology, where, since 2008, he served as a research leader in the study of gene regulation. Using experimental approaches in embryology, molecular biology, and computational biology, he has explored the principles by which developmental pathways evolve.

DEBRA PATT was named editor-in-chief of **JCO Clinical Cancer Informatics**, a new publication of the American Society of Clinical Oncology.

Patt, who specializes in medical oncology and hematology, is a vice president of Texas Oncology, and medical director of outcomes research and the pathways task force for The US Oncology Network. She was formerly medical director of healthcare informatics for McKesson Specialty Health. Her primary research interests are in health services research, health economics outcomes research, and health policy.

JCO CCI will be a peer-reviewed, interdisciplinary journal publishing clinically relevant research covering policy, healthcare services delivery, and clinical insights based on biomedical informatics methods and processes applied to cancer-related data. The first issue of the journal is scheduled to be published later this year.

"We are pleased to have Dr. Patt overseeing this new ASCO journal which is focused on one of the most promising new fields in health care," said ASCO Chief Executive Officer Allen Lichter. "Her unique qualifications and expertise make her the ideal physician editor to take this journal from a concept to a world-class publication."

JENNIE CREWS was elected president of the **Association of Community Cancer Centers** during the association's 42nd annual meeting, in Washington, D.C.

Crews brings more than 18 years of experience in advancing quality oncology care, currently as the medical director for cancer services in the PeaceHealth Northwest Network, which includes cancer centers in Washington state and Alaska. Crews hopes to build on her predecessors' contributions with a theme focused on patient-centered care titled, "Empowering Patients, Engaging Providers."

Crews has been an active member of ACCC, serving as president elect for the past year, and previously as ACCC treasurer. Crews serves as a member of the task force for the ACCC Oncology Drug Database and on the Advisory Committee for the Institute for Clinical Immuno-Oncology, an institute of ACCC.

Previously, Crews was the medical director of the Marion L. Shepard Cancer Center, and held appointments as a consulting associate in the Department of Medicine at Duke University, and as an affiliate associate professor in the Department of Medicine at East Carolina University.

She is a fellow in the American College of Physicians and is board certified in internal medicine and medical oncology. Crews has served as the president of the North Carolina Oncology Association and as the NCOA Legislative Liaison to the North Carolina General Assembly. She is a reviewer for the Journal of Oncology Practice and co-chair of the ASCO Practice Guidelines Implementation Network.

CHARLES SERHAN received the Ross Prize in Molecular Medicine from the **Feinstein Institute for Medical Research**.

Serhan is director of the Center for Experimental Therapeutics and Reperfusion Injury at Brigham and Women's Hospital, the Simon Gelman Professor of Anaesthesia at Harvard Medical School and professor at Harvard School of Dental Medicine.

Serhan's research focuses on structural elucidation of bioactive molecules that activate the resolution of acute inflammation. His laboratory's mission is to identify novel mediators, pathways, and cellular targets critical in promoting resolution of inflammation and reperfusion tissue injury and their relation to human disease.

The Ross Prize is awarded through the Feinstein Institute Press's peer-reviewed journal, Molecular Medicine. The prize, which includes $50,000, will be formally presented June 13 at the New York Academy of Sciences, followed by lectures from Serhan and other researchers.

"Charles Serhan's multidisciplinary approach to science enabled his discovery of resolvins," said Kevin Tracey, Feinstein Institute president and CEO, who also serves as editor emeritus of Molecular Medicine. "These molecular mechanisms hold promise for developing novel approaches to treating inflammation."

THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY published **The State of Cancer Care in America: 2016**, in the Journal of Oncology Practice—ASCO's third annual assessment of national trends in cancer care delivery. The report was also presented at a Congressional briefing in Washington, D.C.,

The report highlights many promising cancer care developments, including new drugs and technologies, declining mortality rates, expanded access to healthcare generally, and a shift towards value-based care. But ASCO also highlights major challenges for patients and physicians, including uneven health insurance coverage, rapidly rising costs, and other barriers to accessing new treatments.

"Continued scientific and medical progress is urgently needed to improve cancer care, but treatment advances will only be as good as our ability to deliver them to patients," said ASCO President Julie Vose. "If we hope to achieve Vice President Biden's goal of doubling the pace of progress, the work of strengthening cancer care delivery has to be pursued just as aggressively as the cancer research agenda."

The ASCO report highlights the continued decrease in cancer incidence and mortality rates for key cancers. This progress can be attributed in part to the growing number of novel drugs and technologies, fueled by the nation's investment in cancer research.

In 2015, the FDA approved 15 new cancer drugs, as well as the first biosimilar to an existing biological product. FDA also approved several screening and diagnostic tests to help better identify cancers at an early stage, target treatments, and improve outcomes for patients.

The nation is also recommitting significant resources to cancer research after a ten-year period of stagnant funding: Congress took an important first step by increasing FY2016 federal cancer research funding by 5.34 percent over the previous year; and the government's moonshot initiative would commit over $700 million and pursue new collaborations to

accelerate progress.

Although patients face better treatment prospects than ever before, the report cautions that cancer care may be compromised due to the growing complexity of care delivery, inadequate healthcare access and affordability, and other external practice pressures.

The report highlights a number of issues:

● Increasing complexity of care delivery—The evolving scientific evidence around individual risk of developing cancer and frequent revisions to screening guidelines, the rapidly advancing field of precision medicine, and an aging U.S. population with changing treatment and other chronic health needs pose new challenges for physicians as they work to deliver consistently high-quality care.

● Remaining gaps in insurance coverage—The Affordable Care Act has enrolled 17 million Americans, and includes a number of provisions that benefit people with cancer. However, approximately 35 million non-elderly adults remain uninsured, 31 million more are underinsured, and Medicaid expansion is still incomplete. A survey of clinical trial sites also found persistent denials of coverage for the routine costs of clinical trials, despite the Affordable Care Act coverage requirement.

● Rising cost of cancer care—The escalating cost of cancer care is having an enormous impact on people with cancer and their families. Some estimates suggest that 10 to 20 percent of patients with cancer may not take prescribed treatments because of cost, putting them at risk for poor cancer outcomes and making them more likely to declare bankruptcy than those without cancer.

● Looming access issues—Three noted trends may impede future access to high-quality cancer care, including: an imbalance between the number of U.S. oncologists practicing in and number of Americans living in rural areas (5.6 percent and 11 percent, respectively); a dramatic increase in the number of cancer patients, a 45 percent increase from 2010 to 2030, largely due to the aging of the U.S. population; and an aging oncology workforce, with 20 percent of oncologists now over the age of 64, and the expected growth in the number of oncologists by 2030 not expected to match the growth in patients.

● Inconsistent adoption, lack of interoperability of health IT—With the potential to significantly improve the quality of cancer care, the integration of electronic health records (EHRs) has led to significant administrative burdens that reduce physicians' available time for patient care, research, teaching, and other professional activities. In fact, nearly half (45 percent) of oncology practices surveyed by ASCO cited EHR implementation as the leading practice pressure, surpassing all other pressures in 2015. Further, the common incompatibility of different health IT systems used by providers inhibits the sharing of information that is needed for optimal cancer care.

The report recommends expanding publicly funded insurance programs to offer consistent and adequate benefits to people living with cancer; testing multiple payment and care delivery models to identify effective solutions; improving value in cancer care by working with stakeholders to develop alternate payment models, as well as clinical guidelines and resources that can help reduce waste and avoid inappropriate treatment; and advancing health information technology that supports efficient, coordinated care, such as electronic health records.

THE V FOUNDATION for Cancer Research and the **WWE** announced a multi-year partnership to support cancer research nationally through funds raised by **Connor's Cure.**

The announcement was made at Children's Hospital of Pittsburgh, where Connor's Cure was originally established, with representatives from the hospital, the WWE and The V Foundation. In 2014, Connor's Cure was created by WWE Chief Brand Officer Stephanie McMahon and WWE's executive vice president of talent, live events and creative, Paul "Triple H" Levesque, as a fund within Children's Hospital of Pittsburgh Foundation to support pediatric brain and spinal cord cancer research.

The new partnership will expand Connor's Cure outside of Children's Hospital of Pittsburgh Foundation and support top research centers and hospitals nationwide. Connor's Cure was established in honor of 8-year-old WWE fan Connor Michalek, a patient at Children's Hospital of Pittsburgh of UPMC who battled medulloblastoma, a rare tumor that affects the brain and spinal cord. To date, Connor's Cure has raised nearly $1 million and assisted more than 100 families around the world.

As a result of the new partnership, funds raised by WWE will support Connor's Cure through The V Foundation's grant-making process. In addition, funding will continue to support the research being done at Children's Hospital of Pittsburgh of UPMC.

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PROVIDENCE HEALTH & SERVICES and the **Institute for Systems Biology** announced an affiliation focused on personalized medicine.

Leroy Hood, will serve as senior vice president and chief science officer of Providence Health & Services, a five-state, not-for-profit health system, and continue as president of the Seattle-based ISB.

Providence and ISB will establish a number of joint research projects in scientific wellness, employing the approach of dense, dynamic personalized data clouds, including: following and understanding early transitions from wellness to disease; analyzing patient populations longitudinally that are at risk for Alzheimer's; helping breast cancer patients recover from illness following debilitating therapies; and utilizing novel approaches to successfully treat glioblastoma, an inevitably fatal type of brain tumor.

ISB's goal is to develop metrics to quantify scientific wellness and identify the earliest markers of transition for all common diseases. ISB will remain a separate legal entity with its own brand and identity and board of directors.

Drugs and Targets

Gilead Halts 6 Zydelig Trials As FDA, EMA Warn of Deaths From Respiratory Infections

FDA is alerting health care professionals about reports of an increased rate of adverse events, including deaths, in clinical trials with the cancer medicine Zydelig (idelalisib) in combination with other cancer medicines.

Gilead Sciences Inc. stopped six clinical trials involving Zydelig, in patients with chronic lymphocytic leukemia, small lymphocytic lymphoma and indolent non-Hodgkin lymphomas. The FDA said it is reviewing the findings of the clinical trials and will communicate new information as necessary. Health care professionals should be aware that Zydelig is not approved for previously untreated chronic lymphocytic leukemia, the agency said.

The FDA is urging health care professionals and patients to report adverse events involving Zydelig to the FDA MedWatch program.

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee issued provisional advice for doctors and patients, while the medicine is being reviewed, to ensure that it continues to be used as safely as possible. Zydelig is currently authorized in the EU to treat chronic lymphocytic leukemia and follicular lymphoma.

The committee recommends that all patients treated with Zydelig should receive antibiotics to prevent a particular type of lung infection, Pneumocystisjirovecii pneumonia. Patients should also be monitored for infection and have regular blood tests for white cell counts because low counts can increase their risk of infection. Zydelig should not be started in patients with a generalized infection. It should also not be started in previously untreated patients with CLL whose cancer cells have certain genetic mutations (17p deletion or TP53 mutation), the committee said.

Zydelig is currently approved by the FDA for the treatment of relapsed chronic lymphocytic leukemia, in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities; relapsed follicular B-cell non-Hodgkin lymphoma in patients who have received at least two prior systemic therapies; and relapsed small lymphocytic lymphoma in patients who have received at least two prior systemic therapies.

FDA granted an Orphan Drug Designation to VAL-083 for the treatment of medulloblastoma. The investigational drug candidate, developed by DelMar Pharmaceuticals Inc., previously received an orphan designation for glioblastoma in the U.S. and in Europe.

VAL-083 is a first-in-class chemotherapeutic. In more than 40 phase I and II clinical studies sponsored by the NCI, VAL-083 demonstrated clinical activity against a range of cancers including lung, brain, cervical, ovarian tumors and leukemia both as a single-agent and in combination with other treatments.

In historical NCI-sponsored clinical studies, VAL-083 demonstrated clinical activity against medulloblastoma. In these studies VAL-083 was investigated both as a stand-alone therapy and in combination with other chemotherapeutic regimens. DelMar's recent pre-clinical research demonstrates that VAL-083 is active against medulloblastoma cells with difficult to treat sonic hedgehog characteristics and p53 mutations; and VAL-083 in combination with temozolomide completely inhibits self-renewal of pediatric brain cancer stem cells.

Additionally, DelMar has been conducting clinical trials with VAL-083 as a potential treatment for glioblastoma multiforme. In September 2015, DelMar announced completion of enrollment in a phase II clinical trial in refractory GBM. The company anticipates top-line overall survival data from this trial in the first half of this year.

FDA granted Priority Review for atezolizumab (anti-PDL1; MPDL3280A) for the treatment of people with locally advanced or metastatic urothelial carcinoma who had disease progression during or following platinum-based chemotherapy in the metastatic setting, or whose disease worsened within 12 months of receiving platinum-based chemotherapy before or after surgery.

"Atezolizumab was granted Priority Review designation based on results of the IMvigor 210 study, which showed the medicine shrank tumors in a type of advanced bladder cancer, and the majority responding to treatment continued to respond after nearly a year of follow up," said Sandra Horning, chief medical officer and head of Global Product Development at Genentech, the drug's sponsor. "The treatment options available for advanced bladder cancer are very limited, and we are committed to working with the FDA to bring the first anti-PDL1 cancer immunotherapy to people with this disease as quickly as possible."

IMvigor 210 is an open-label, multicenter, single-arm phase II study that evaluated the safety and efficacy of atezolizumab in people with locally advanced or mUC, regardless of PD-L1 expression. People in the study whose disease had progressed during or following previous treatment with a platinum-based chemotherapy regimen (n=311) received a 1200-mg intravenous dose of atezolizumab on day one of 21-day cycles until loss of clinical benefit. The primary endpoint of the study was objective response rate as assessed by an independent review facility. Secondary endpoints included duration of response, overall survival, progression-free survival and safety.

In an updated analysis based on 11.7 months of median follow up, atezolizumab shrank tumors in 15 percent (95% CI: 11, 19) of people evaluable for efficacy and safety (n=310) whose disease progressed after platinum-based chemotherapy.

Atezolizumab shrank tumors in 26 percent (95% CI: 18, 36) of people whose disease had medium and high levels of PD-L1 expression. Median duration of response was not reached at the time of analysis; with a median duration of follow up of 11.7 months, 84 percent of people had an ongoing response.

Genentech also has an ongoing, confirmatory phase III study (IMvigor 211), which compares atezolizumab to chemotherapy in people whose bladder cancer has progressed on at least one prior platinum-containing regimen.