# THE CANCER LETTER

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## Timeline Pinpoints the Role of Cancer Scandal In a Progression Leading to Perry's Indictment

*By Paul Goldberg*

The indictment of Texas Governor Rick Perry by a Travis County grand jury brings together two complex subplots:

• The controversy over the Cancer Prevention and Research Institute of Texas, which came into public view May 8, 2012, with the resignation of its scientific leader, Nobel Laureate Alfred Gilman, who claimed that political interference had caused a departure from standard peer review in the handling of a proposal to fund a $20 million "biotechnology incubator" at MD Anderson Cancer Center, triggering a delay in funding of previously reviewed grants.

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## Device Maker Threatens Legal Action Against Doctor Who Launched Campaign to End Power Morcellation

*By Paul Goldberg and Matthew Bin Han Ong*

A German company that makes devices now under FDA scrutiny for their potential to spread sarcoma threatened legal action against the U.S. surgeon whose wife's cancer cells were disseminated during routine surgery to remove fibroids.

Setting decorum aside, Hooman Noorchashm has been haranguing FDA, Congress, and the gynecology and oncology profession into partial abandonment of the procedure.

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## George Weiner to be President of AACI; Stanton Gerson Chosen as President-elect

**GEORGE WEINER** will begin a two-year term as president of the Association of American Cancer Institutes following its annual meeting in Chicago, Oct. 26-28.

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## Events at Center of Indictment Occured During Probe of CPRIT

(Continued from page 1)

• The political wrangling that followed the April 12, 2013, drunk driving arrest of Travis County District Attorney Rosemary Lehmberg, whose duties include administering the Public Integrity Unit, which investigates corruption of state officials.

The plot lines crossed on Dec. 7, 2012, when the Travis County DA initiated a criminal investigation of CPRIT, and they stayed together through the Dec. 3, 2013 indictment of CPRIT's chief commercialization officer, Jerald Cobbs, on charges stemming from his failure to conduct peer review of a proposal before awarding $11 million in Texas taxpayers' money.

The case was unrelated to the MD Anderson-led incubator. Cobbs's trial is expected to begin later this year.

The CPRIT issue has become important because attorneys defending Perry on felony charges of abuse of official capacity and coercion of a public servant have made efforts to defuse it.

"The CPRIT issue the Democrats are trying to peddle is a red herring and a phony issue," Benjamin Ginsberg, the governor's attorney, said in a recent telephone conference with reporters. The Perry defense team said they have obtained an affidavit in which a former Travis County Public Integrity Unit investigator said that the governor was not the target of the CPRIT investigation.

CPRIT is a taxpayer-funded initiative that dispenses $300 million a year in state funds for cancer causes.

To examine the plausibility of the issues that emerged in the context of the CPRIT investigation playing a role in the case against Perry, The Cancer Letter put together a timeline that reflects development of these two subplots. The timeline combines legal and political analysis with detailed coverage of controversies at CPRIT and MD Anderson in an effort to examine their potential role in Perry's indictment.

At the time Lehmberg saw the lights of a police cruiser, her office was going into the fifth month of investigation of irregularities at CPRIT.

That probe involved examination of the role played by at least one major Republican donor—Charles Tate—who emerged as a central figure in the MD Anderson incubator controversy.

Tate's role can be traced through thousands of pages of documents obtained by The Cancer Letter and several Texas newspapers.

Also, the timeline shows that prosecutors at the Travis County Public Integrity Unit pressed forward on the CPRIT case even after Perry vetoed the state contribution to the prosecutors' budget, causing a reduction in workforce and a scramble for funds.

Most importantly, during the eight months that elapsed between Lehmberg's drunk driving scandal and the Cobbs indictment, no one outside the investigation could have been expected to have the capability to gauge the direction of the probe.

Yet, even those tracking the investigation from the sidelines would have been able to see that Travis County investigators, as they conducted interviews, were focusing on some of the most important players in Texas politics.

Consider Tate. A list of his contributions to candidates and political action committees can be found through a simple search of the Texas Ethics Commission website. His beneficiaries include the governor, the lieutenant governor, and the state attorney general, to name a few.

As prosecutors announced the Cobbs indictment, they stated that no further prosecution would be expected in the CPRIT case. However, this doesn't rule out the possibility that CPRIT figures in the Perry indictment. This is because the Cobbs case turns on whether peer review of a grant proposal was ever conducted, while the Perry case is about exercise of undue influence.

In these two different contexts, the same facts can

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have very different implications.

By establishing the flow of events, timelines can be used to rule out implausible hypotheses. Nobody outside the investigation knows precisely what the grand jury saw. However, based on analysis of the progression of events, the hypothesis that the CPRIT investigation figured in the events that led to Perry's indictment cannot be eliminated.

**Cobbs, Lehmberg and Perry**

Travis County, a blue stronghold in a red state, operates the corruption investigations unit, which many state politicians wish to transfer to the office of the attorney general.

Lehmberg's drunk driving arrest and less than decorous behavior, which was captured on camera and posted on the Internet, was a godsend to anyone wishing to weaken her office.

Though Lehmberg's anti-corruption office has prosecuted more Democrats than Republicans, one of its biggest successes was the conviction of another national Republican figure, former Rep. Tom DeLay, who was convicted on criminal charges of conspiracy to violate election law. (The judgment was later overturned by a higher court, and the dismissal of the case is under review by the Texas Court of Criminal Appeals.)

Several CPRIT insiders characterized Cobbs, the indicted CPRIT official, as a functionary directed by a "commercialization" panel—the panel headed by Tate.

Internal CPRIT emails obtained by The Cancer Letter show that Tate played a key role in devising the MD Anderson proposal for a biotech incubator and moving it through the system (The Cancer Letter, Sept. 28, 2012).

The MD Anderson controversy didn't figure in the Cobbs indictment. The former official was charged with securing execution of a document by deception, a first-degree felony.

It's not publicly known why Cobbs didn't conduct a formal review of the $11 million funding proposal from a company called Peloton Therapeutics Inc. of Dallas before deciding to award the grant in 2011.

No information has emerged to suggest that Peloton officials have sought special treatment, or that the company's science would not have withstood scrutiny. In fact, the company's science has survived due diligence performed by The Column Group, a venture capital firm that led a Series A financing round investing $18 million in the startup.

Also, Texas billionaire Peter O'Donnell—whose foundation picked up a portion of the salaries of CPRIT officials, and paid for dinners of peer reviewers—was among those investing in Peloton. However, sources say that O'Donnell bought Peloton stock well after the company was funded, and then transferred stock ownership to UT Southwestern.

The stakes in the CPRIT controversy were high: nearly all of the $300 million CPRIT was dispensing every year went through a rigorous peer review system engineered by Gilman.

Under Gilman's stewardship, CPRIT didn't promise the cures. Rather, the institute promised well-run study sections that funded good science.

Meanwhile, MD Anderson President Ronald DePinho, then a newcomer to Texas, was seeking to use a portion of CPRIT funds for his $3 billion "Moon Shots Program" to eventually eradicate eight cancers (The Cancer Letter, Sept. 7, 2012, Sept. 21, 2012).

After quitting CPRIT, Gilman and his former chief scientific advisor Phillip Sharp, a fellow Nobel laureate, offered words of caution to guide CPRIT (The Cancer Letter, Oct. 19, 2012).

"Reliance on peer review to identify the best science must continue to guide CPRIT in the future," Gilman and Sharp wrote. "Of course, there are other ways to distribute public funds, but they are worse. Their side effects include infamy and they end in irrelevance."

Top Texas officials didn't seem to feel the sting of Gilman and Sharp's words. In a joint letter, three politicos promised to go beyond funding basic science and place an increased emphasis of commercial projects (The Cancer Letter, Oct. 26, 2012).

"It is now time for CPRIT to take further steps to fulfill its statutory mission and expedite innovation that will deliver new cancer treatments to patients within three to five years," the three officials said in a letter.

The troika included Speaker of the House Joe Strauss, Lieutenant Governor David Dewhurst—and Governor Perry.

## The Timeline:

This timeline draws on over two years of The Cancer Letter's coverage of the controversy at the Cancer Prevention and Research Institute of Texas and MD Anderson Cancer Center.

The objective is to enrich the existing timelines that have been put together by The Texas Tribune and Texas Lawyer and examine the role the CPRIT and MD Anderson controversies may have played in the indictment of Texas Governor Rick Perry.

• **May 8, 2012:** Alfred Gilman, a Nobel laureate, submits a letter of resignation from his position as chief scientific officer of the Cancer Prevention and Research Institute of Texas.

His resignation is triggered by two events:

• Efforts to fund a $20 million biotechnology incubator led by MD Anderson Cancer Center. Gilman contends that the proposal is a scientific project disguised as a commercialization project and that it has to go through scientific review. The proposal's proponents say that it doesn't.

• Failure to fund multi-institution grants that had previously gone through successful peer review (The Cancer Letter, May 25, 2012).

This is the first time the public learns about irregularities at CPRIT.

By turning whistleblower, Gilman brings into focus efforts by top Texas officials to shift CPRIT's emphasis from peer reviewed research to commercial projects.

Documents subsequently obtained by The Cancer Letter show a deep rift between basic science and commercialization efforts, focusing on the role played by Tate, the Texas financier, Republican donor, and chief of the CPRIT commercialization panel.

Tate was involved in formulating the proposal for the MD Anderson-led incubator. The key meetings included MD Anderson President Ronald DePinho and his wife Lynda Chin, a senior scientist at MD Anderson (The Cancer Letter, Sept. 28, 2012).

• **March 29, 2012:** The CPRIT Oversight Committee approves funding for a $20 million biotech incubator co-directed by MD Anderson and Rice University.

The money was intended to fund the MD Anderson Institute for Applied Cancer Science, which is, in effect, functions a lot like a drug company operating within the cancer center. The idea behind the institute is to be able to move rapidly to start—and discontinue—projects.

Tate was the author of an earlier plan to exempt technology incubators from scientific review.

In emails obtained by The Cancer Letter, Chin said that the decision to combine the Rice and MD Anderson proposals was made on Dec. 1, 2011, at a meeting with Tate.

Emails show that Jerald Cobbs was the official who received the proposal from MD Anderson's IACS. The proposal was sent to Cobbs as an attachment to an email from an official at MD Anderson.

The proposal appears to depart from two standard procedures for submission or research grants: (1) it was never reviewed by the MD Anderson provost; and (2) it went directly to Cobbs, bypassing the CPRIT portal, which must be used for submission of applications.

Prior to submission—in early March 2012—Cobbs asked Gilman to look over the IACS proposal. Gilman said that the document lacked scientific content: there were no targets mentioned, no molecules, no diseases, and no intellectual property. There was nothing to review.

Gilman said the proposal should be submitted as a large, multi-investigator grant, accompanied by sufficient detail. Cobbs concurred, telling Gilman that the Chin proposal would go nowhere, at least until the problems are resolved.

Documents show that, unbeknownst to Gilman, Tate was working on a plan to combine the proposals and get them to oversight committee.

On March 14, 2012, in an email to Cobbs, CPRIT Executive Director Bill Gimson stated that Tate had warned him about considering the Rice proposal first, to be followed by the MD Anderson proposal: "Jerry: Charles just called me—he is concerned about timing and bifurcated approach of the Rice/IACS Incubator."

Even though funding for the MD Anderson-led project was approved, no money changed hands.

• **Oct. 12, 2012:** Gilman leaves CPRIT. Many top-level scientists who participated in the study sections follow, submitting blistering letters of resignation (The Cancer Letter, Oct. 12, 2012, Oct. 26, 2012).

• **Nov. 16, 2012:** Cobbs unexpectedly resigns as chief commercialization officer of CPRIT, stating that he plans to return to the private sector. The agency officials declined to elaborate on the departure, initially describing it as a "personnel matter" (The Cancer Letter, Nov. 30, 2012).

• **Nov. 29, 2012:** The Peloton problem is announced in a press release. CPRIT officials state that, in the course of a compliance review, they discovered that the company's proposal received $11 million without any peer review.

The state agency said it has notified Peloton and placed a hold on future funding (The Cancer Letter, Nov. 30, 2012).

• **Nov. 30, 2012:** Two state legislators who wrote the legislation that created CPRIT write a letter to express "deep concern" about the agency funding a grant to Peloton without formal peer review.

"As the authors of the original CPRIT statute—and subsequent legislation to strengthen the institute's guidelines to ensure transparency and prevent conflicts of interest—we require an explanation in writing as to how this occurred. That explanation should include a description of what occurred, when and how the problem was discovered, what actions have been taken to rectify the situation, and how CPRIT proposes to prevent such oversight from occurring in the future," wrote State Sen. Jane Nelson (R-Flower Mound) and Rep. Jim Keffer, (R-Eastland) in a letter to CPRIT (The Cancer Letter, Dec. 14, 2012).

• **Dec. 7, 2012:** The Travis County district attorney opens a criminal investigation of the "award of grants" by CPRIT. No grant is specified. The matter is assigned to the Public Integrity Unit. (The Cancer Letter, Dec. 14, 2012).

• **Dec. 8, 2012:** CPRIT Oversight Committee Chairman Jimmy Mansour asks for an investigation by the Texas attorney general and an audit by Deloitte Touche. His email to CPRIT Executive Director Bill Gimson reads: "Please contact the Attorney General's office and request that he direct his attorneys to seek affidavits from all individuals related to or associated with Peloton past and present. Please encourage them to return to us as soon as possible. Please contact the Governor's Office requesting an emergency waiver approval for an audit of CPRIT by Deloitte Touche. Please contact DIR and request forensic assistance in recovering all lost email between Gerry Cobb, Al Gilman and Bob Ulrich relating to [Peloton]. Also, please send this note to the Board."

A subsequent email reads: "We need to know if they have any financial interest in Peloton or benefited in some related way from it receiving approval."

• **Dec. 10, 2012:** CPRIT Executive Director Gimson submits a letter of resignation. Margaret Kripke's acceptance of the job of CPRIT chief scientific officer is announced (The Cancer Letter, Dec. 14, 2012).

Texas Attorney General Greg Abbott informs CPRIT that it has opened an inquiry into "the flawed grant that [CPRIT] awarded to Peloton Therapeutics."

The letter states that "the review will include—but is not limited to—any financial interest CPRIT staff or any other individual may have had in the Peloton grant award. Abbott was a member of the CPRIT oversight committee. (The Cancer Letter, Dec. 14, 2012). The investigation hasn't resulted in any actions.

• **April 12, 2013:** Travis County District Attorney Rosemary Lehmberg is charged with driving while intoxicated. She was traveling in the bike lane for a mile. An open bottle of vodka is found in the car's passenger area.

• **April 19, 2013:** Lehmberg pleads guilty to a misdemeanor and begins a 45-day sentence in jail.

• **April 29, 2013:** Travis County Attorney David Escamilla files a lawsuit seeking to remove Lehmberg from office because of the drunk driving incident.

• **May 24, 2013:** Lehmberg counters by claiming that the Texas statute that enables removal of government officials for drunkenness is unconstitutional. Also, habitual drunkenness—as opposed to one incident—should be required.

• **June 17, 2013:** A line-item veto by Perry strikes $7.57 million in funds for the Public Integrity Unit of the Travis County District Attorney Office. Perry says he denied state funding because Lehmberg had "lost public confidence."

• **July 2, 2013:** The Travis County Commissioners Court vote to send "reduction in force" notices to over 30 employees of the Public Integrity Unit, effective Sept. 30, 2013. The jobs are being eliminated because Perry had vetoed the funding.

• **July 8, 2013:** San Antonio lawyer Michael McCrum, former DA of Brazos County, is appointed to investigate a criminal complaint against Lehmberg. The allegation: Lehmberg committed a felony when she threatened jailers following her DWI arrest.

McCrum, whose political leanings are unclear, was appointed by Judge Bert Richardson, who continues to preside over the case.

Richardson, a Bush appointee, identifies himself as a conservative. He serves as a senior judge in regions spanning the area from San Antonio to Del Rio and Austin to El Paso.

In his current campaign for a seat on the Court of Criminal Appeals, Richardson has the endorsements of groups that include Conservative Republicans of Texas,

Kaufman County Tea Party, and the Texas Coalition of Christian Candidates.

• **Aug. 12, 2013:** The Travis County commissioners direct the budget office to move $1.76 million to the Travis County District Attorney's Public Integrity Unit. Lehmberg will also contribute $734,000 from another account.

• **Aug. 19, 2013:** McCrum takes the oath to investigate whether Gov. Perry committed crimes when he vetoed funding for the Travis County Public Integrity Unit.

• **Sept. 6, 2013:** The judge overseeing the criminal complaint against Perry chooses members of the grand jury.

• **Oct. 4, 2013:** A grand jury declines to indict Lehmberg on a complaint that she committed a felony when she threatened jailers following her drunk driving arrest.

• **Dec. 3, 2013:** A grand jury in Travis County indicts Cobbs for bypassing peer review in awarding an $11 million grant to Dallas-based Peloton.

Announcing the Cobbs indictment, Travis County Assistant District Attorney Rob Drummond says that the grand jury was asked to review the materials stemming from the MD Anderson IACS controversy and materials related to CTNeT, a now-defunct statewide network focused on cancer clinical trials. "The grand jury didn't choose to issue indictments related to those matters," Drummond said (The Cancer Letter, Dec. 17, 2013).

The Public Integrity Unit also investigated the allegations of conflicts of interest and financial improprieties related to the CPRIT Foundation, and conflicts related to the business interests of members of CPRIT's oversight committee. However, these matters were not presented to the grand jury, Drummond said. Investigators saw no fault on the part of Peloton.

"No charges were considered against anyone connected to Peloton," Drummond said. "The evidence indicated that they were unaware that their grant award had bypassed the required review committees."

The company received a portion of the $11 million awarded by the state, and has since reapplied to receive the rest of the funds, but has not as yet received any additional funding.

Peloton was founded by Steven McKnight, who holds the Distinguished Chair in Basic Biomedical Research and the Sam G. Winstead and F. Andrew Bell Distinguished Chair in Biochemistry at UT Southwestern. He is a member of the National Academy of Sciences.

Prosecutors said they would seek no additional indictments on matters connected to CPRIT.

• **Dec. 11, 2013:** Visiting Judge David Peeples denies the state's petition to remove Lehmberg from office.

• **Aug. 15, 2014:** A Travis County grand jury indicts Gov. Perry for two felony counts: abuse of official capacity and coercion of a public servant.

In a statement issued the next day, Perry says he is a victim of political prosecution:

"This indictment amounts to nothing more than an abuse of power and I cannot, and will not, allow that to happen. I intend to fight against those who would erode our state's constitution and laws purely for political purposes, and I intend to win. I will explore every legal avenue to expedite this matter and bring it to a swift conclusion. I am confident we will ultimately prevail, that this farce of a prosecution will be revealed for what it is, and that those responsible will be held to account."

• **Aug. 19, 2014:** Perry is booked.

## CPRIT Awards Round of Grants

The Cancer Prevention and Research Institute of Texas last month awarded 101 new grants: 84 for research, 15 for prevention and two for product development.

CPRIT received nearly 600 grant applications, and after review, awarded grants to cancer researchers, prevention initiatives and product development projects from institutions and organizations across the state.

• The research grants added up to $76.2 million, supporting 76 research projects and the recruitment of eight cancer scientists and clinicians to academic institutions in Texas.

• The prevention awards added up to $17.5 million. The projects will support prevention services for underserved populations, focusing on HPV vaccination rates, tobacco cessation in young adult smokers and increasing access to colorectal cancer screening.

• The $13.5 million of two product development grants will support cancer research and development conducted by a Texas-based company and the relocation of an existing cancer-focused company to Texas. The grants will fund projects to develop novel brain cancer treatments and advanced imaging and diagnostic techniques.

With this $107.2 million in grants, CPRIT has given out a total of $970 million in Texas taxpayers' money. Altogether, the state institution was authorized to spend $3 billion over a decade.

Following a series of scandals in 2012, Texas officials imposed a moratorium on CPRIT's grant-making. That moratorium was lifted in October 2013, after new members were appointed to the CPRIT oversight committee.

CPRIT, which pays as much in cancer research grants as the federal government within the state, reactivated grant-making in November 2013. The organization has reconstituted its scientific review mechanism after many reviewers resigned in protest over the decision to award of a "commercialization" grant to MD Anderson Cancer Center.

The most recent round of grants is the second since the moratorium. A list of these awards is posted on CPRIT's website.

## Karl Storz Threatens Lawsuit Against Doctor Who Brought Morcellation Dangers to Light

(Continued from page 1)

Though he hasn't sued anyone, several law firms are looking for women harmed by the procedure who would be willing to take part in litigation.

As an apparent result of this campaign by Noorchashm and his wife Amy Reed, top institutions—including Brigham and Women's Hospital, where Reed underwent the procedure—are moving away from routine use of morcellation, and some insurers are refusing to pay for the procedure.

One of the largest manufacturers of these devices—Ethicon, a unit of Johnson & Johnson—recently voluntarily withdrew the devices, which cost between $1,500 and $3,000 each.

Power morcellation is performed on an estimated 100,000 women in the U.S. a year with a minimally invasive device that pulverizes a patient's fibroids into fragments for easy removal through a small incision. The problems occur when power morcellators disseminate cells from undetected cancers.

The Karl Storz Group, the company that Noorchashm says made the device that was used in Reed's surgery, is taking a different approach.

In a letter, the company said it wasn't its device that made Reed ill; her sarcoma was present before the surgery.

And, citing Noorchashm's emails, a Karl Storz official warned him to cease his campaign against power morcellation or face legal action.

"KARL STORZ insists that you immediately stop your campaign against the Rotocut morcellator, and any other morcellator device of KARL STORZ, and that you stop defaming the device and/or the KARL STORZ management in the medical world or on the market place," the letter states.

"We will no longer tolerate unfounded and unproven allegations such as the ones contained in your previous emails and we will hold you responsible. Should we get to know further public statements from you that our device and/or management would be responsible for your wife's and/or other women's uterine cancer, and/or aggravation of their cancerous situations, we would not hesitate to take appropriate legal actions to protect our good name and our rights.

"We trust that you understand our position and conclude by wishing you and your wife that you win your battle against the shocking illness which, nevertheless, cannot be attributed to any of our devices or acts."

The letter, dated Aug. 22, is signed by Helmut Wehrstein, a member of the global executive committee of the company based in Tuttlingen, Germany.

Noorchashm says he has no plans to stop.

"This letter exemplifies an entire industry's sentiments towards a deadly iatrogenic women's health hazard—namely, upstaging of gynecological cancers using morcellators," said Noorchashm, who is in the process of moving from Harvard to the Thomas Jefferson Medical College Department of Surgery. "Clearly, almost all morcellator companies, including Storz, had recognized that their devices have the potential to spread and upstage cancerous tissues—many of their user's manuals stated as such.

"Of course, almost all gynecological surgeons also recognized this avoidable peril, but seem to have accepted the collateral damage for the 'benefit of the majority.' Yet, none of the manufacturers or gynecological surgeons worldwide had reported this hazard to FDA until I did so in December of 2013, from my wife's bedside, after she had undergone a major operation to remove the morcellated bits of leiomyosarcoma in her pelvic cavity.

"And now, I receive this bold letter in response to our appropriately loud alarm of public hazard, threatening legal action against me. How incredible! A Storz morcellator is used by a gynecological surgeon in Boston and causes my wife's cancer to be spread inside her abdominal cavity, the company knows that this potentially deadly complication could occur, yet it continues to sell the product worldwide.

"And in response to my call to corporate responsibility and request that the company's leadership act in the best interest of patient safety, I get a letter threatening legal action. Incredible!

"This specific example is why it 100% imperative that the United States Food and Drug Administration step up to the plate and regulate all these morcellator devices definitively. This specific example is also why the U.S. Congress must act to correct the 510(k) legislation governing medical device approval.

"Corporate responsibility works most of the time. It leads to innovation and progress most of the time. But when it fails, and it clearly has in the case of morcellators among a few other examples, the federal government must act, and act well, to protect the public."

FDA has issued a safety communication and convened an advisory panel to solicit advice. Following J&J's decision to withdraw its version of the device, two members of the Senate urged FDA to ask other manufacturers to withdraw the device pending outcome of additional assessment of risk.

"As the FDA prepares to make a final determination on the use of these devices, we urge you to seriously consider and not discount the testimony presented during the FDA's July hearings by our constituents who devastatingly lost family members to cancer after a power morcellation procedure," Sens. Kirsten Gillibrand (D-N.Y.) and Charles Schumer (D-N.Y.) wrote in a recent letter to FDA Commissioner Margaret Hamburg.

## "KARL STORZ Insists That You Immediately Stop Your Campaign Against the Rotocut Morcellator"

*The letter sent to Noorchashm follows:*

Dear Dr. Noorchashm,

This refers to several emails which you addressed—amongst others—to Dr. h.c. mult. Sybill Storz, the CEO of the KARL STORZ Group.

In your emails, you requested Dr. Storz to "recall your Rotocut morcellator device from the market", arguing that it caused harm to patients. You also urged Dr. Storz that she "must do right by all those who have been harmed" (21 May 2014) and you sent her (and other recipients) a collage of "30 women, some dead'; calling them "Your victims. Victims of your standard of care and using your robotic a power morcellator devices". Again, in this email (24 June 2014) you imply that the power morcellator was the cause of some women's deaths.

We know that amongst the 30 women displayed on the mentioned collage, is your wife. We also totally appreciate the shock and the suffering that you both must have had when the unsuspected uterine leiomyosarcoma was diagnosed on her after a laparoscopic treatment with power morcellation. In spite of this, and with a full understanding of your concern that power morcellation may potentially aggravate the cancerous status of a patient with hidden uterine sarcoma, one must distinguish between cause and effect. One thing is clear: Uterine sarcoma is not caused by power morcellation! To stop all morcellation today will not decrease the number of women carrying hidden, lethal uterine sarcomas. Women who happen to have the misfortune of a hidden uterine sarcoma are and have been seriously ill before laparoscopic surgery is or was applied to them. The illness has other causes and is by no means the result of a dangerous or malfunctioning device.

Furthermore, the risk of spreading an undetected cancer by minimal invasive surgery (MIS) must be measured against the benefits and risks of ubiquitous open surgery. The latter is generally associated with higher rates of morbidity and mortality.

MIS has many recognized advantages over open surgery such as: Reduced hemorrhaging (less need for blood transfusions), smaller incisions (reducing pain and recovery time, as well as post-operative scarring), reducing exposure of internal organs to possible external contaminants (thereby lowering the risk of acquiring infections), less pain, less post-operation medication and shorter hospital stay needed (often same day discharge), overall a faster return to everyday living. On the other end of the scale, there is the unquantified—but generally considered to be low—risk of inadvertently disseminating unsuspected malignant tissue in the body.

This may potentially result in the "upstaging" of a tumor and a worsening of a patient's prognosis. But, again, as clearly came out during the recent FDA Obstetrics and Gynecology Devices Panel Hearing, held on 10th and 11th July 2014, it is not the (long tested) morcellator device that causes this problem, but the inability of today's diagnostic medicine to detect, without invasive surgery, aggressive uterine sarcomas and to distinguish them from benign uterine fibroids.

You are assured that KARL STORZ will monitor

the situation closely and will do its best to protect patients against any unnecessary risks. But, at the present stage, and considering the weak data on the specific risks attributable to the morcellation device itself (as opposed to the procedure), KARL STORZ considers it best to wait for the FDA's final conclusions and recommendations and decided not to take a product from the market which, for hundreds and thousands of women, offers a safe and less invasive way for treating fibroids than by open surgery.

Based on the above, KARL STORZ insists that you immediately stop your campaign against the Rotocut morcellator, any other morcellator device of KARL STORZ, and that you stop defaming the device and/or the KARL STORZ management in the medical world or on the market place. We will no longer tolerate unfounded and unproven allegations such as the ones contained in your previous emails and we will hold you responsible.

Should we get to know further public statements from you that our device and/or management would be responsible for your wife's or any other women's uterine cancer, and/or any aggravation of their cancerous situations, we would not hesitate to take appropriate legal actions to protect our good name and our rights.

We trust that you understand our position and conclude by wishing you and your wife that you win the battle against the shocking illness which, nevertheless, cannot be attributed to any of our devices or acts.

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**Read The Cancer Letter's Past Coverage**
**Of the Power Morcellation Controversy**

## NCI Launches ALCHEMIST

NCI launched another in a series of targeted treatment trials referred to as the **A**djuvant **L**ung **C**ancer Enric**h**m**e**nt **M**arker **I**dentification and **S**equencing **T**rial.

ALCHEMIST seeks to identify mutations in early-stage lung cancer patients, and uses this information to assign them to treatments targeted for those mutations.

"We believe that the findings from ALCHEMIST will not only help answer an important question about the addition of targeted therapies in earlier stage disease, but will also help us in understanding the prevalence and natural history of these genomic changes in earlier stage lung cancer," Shakun Malik, head of Thoracic Cancer Therapeutics in the NCI Clinical Investigations Branch, said in a statement. "We also hope to gain a better understanding regarding the genetic changes in the tumor at the time of recurrence.

"The findings will help to define clinical, biologic and molecular behaviors of this type of lung cancer."

ALCHEMIST is coordinated by the Alliance for Clinical Trials in Oncology and the ECOG-ACRIN Cancer Research Group.

All of the NCI-supported National Clinical Trials Network groups collaborated in the development of ALCHEMIST and are participating in the component trials.

Patients enrolled in ALCHEMIST have been diagnosed with lung adenocarcinoma or similar types of lung cancer as identified by examining the tissue; will undergo surgical removal of their tumors; and will need to complete standard therapy after surgery,

consisting of chemotherapy with or without radiation therapy, as prescribed by their physician.

In the ALCHEMIST screening trial, the surgically removed tissue will be tested in a central laboratory for certain genetic changes in two genes, ALK and EGFR.

Participants with tumors found to have EGFR mutations or rearrangement of the ALK gene will then be referred to one of two randomized, placebo-controlled ALCHEMIST treatment trials.

These studies will evaluate the value of adding therapy with specific agents targeted against two genetic alterations—erlotinib for EGFR, and crizotinib for ALK—in the post-operative setting.

FDA has approved these drugs for advanced forms of lung cancer whose tumors harbor the targeted genetic alterations, but it's not known whether these agents will be beneficial in the adjuvant setting.

The goal is to determine whether erlotinib or crizotinib will prevent lung cancer recurrence, as well as prolong life, when used against tumors that carry specific mutations.

The component trials of ALCHEMIST are:

• ALCHEMIST—Screening component (A151216)—Coordinated by the Alliance for Clinical Trials in Oncology. Principal Investigators: Pasi Janne, and Geoffrey Oxnard, Dana-Farber Cancer Institute.

• ALCHEMIST—EGFR Treatment component (A081105)—Coordinated by the Alliance for Clinical Trials in Oncology. Principal Investigator: Ramaswamy Govindan, Washington University.

• ALCHEMIST—ALK Treatment component (E4512)—Coordinated by ECOG-ACRIN. Principal Investigator: David Gerber, University of Texas Southwestern Medical Center at Dallas.

In the U.S., about 10 percent of patients with lung adenocarcinoma and similar types of lung cancer have tumors with alterations in the EGFR gene, and 5 percent have alterations of the ALK gene.

ALCHEMIST will screen about 6,000 to 8,000 potential participants at hundreds of sites across the U.S. over five to six years to identify those with EGFR and ALK alterations who would be eligible for the two ALCHEMIST treatment trials.

The researchers expect a total enrollment of about 800 patients in those treatment trials. All screened participants, irrespective of the marker status of their tumors, will be followed for five years in the screening trial.

At the conclusion of the treatment trials, statisticians will analyze the survival of patients who received an additional genetically-targeted drug therapy versus patients who received standard therapy alone.

For the ALCHEMIST screening component, central laboratory testing for EGFR gene mutations and for the ALK gene rearrangement will be performed by Response Genetics Inc.

For the ALCHEMIST treatment trials, Pfizer will provide crizotinib under a clinical trials agreement with the ECOG-ACRIN Cancer Research Group.

Astellas Pharma US Inc. will provide erlotinib under a cooperative research and development agreement with NCI for the clinical development of erlotinib.

"This approach highlights the ability of NCTN to efficiently screen large numbers of patients in order to identify those with early-stage EGFR mutant or ALK rearranged lung cancer," Monica Bertagnolli, chair of Alliance, said in a statement. "Without this capability, it would be impossible to identify a sufficient number of patients needed to perform clinical trials to determine whether EGFR or ALK inhibitors prolong survival in early-stage lung cancer."

"ALCHEMIST is the first major study for early-stage lung cancer to provide a coordinated approach to molecular screening, deep genetic sequencing, and treatment tailored to specific mutations, i.e. ALK and EGFR," said Robert Comis, group co-chair of ECOG-ACRIN. "In the E4512 trial, we are hopeful that targeting ALK in early stage disease will improve the cure rate in patients harboring this mutation. "

ALCHEMIST incorporates DNA sequencing and genomic analysis of tumor tissue, and possible additional genomic analysis at the time of lung cancer recurrence. Moreover, every participant enrolled in ALCHEMIST will also be studied for cancer risk characteristics, and their tumor tissue will be analyzed with advanced sequencing technologies in a research genomics initiative conducted by the NCI Center for Cancer Genomics.

This research will capitalize on the foundation of CCG's earlier effort, The Cancer Genome Atlas, which is a collaboration with the National Human Genome Research Institute, another component of NIH.

Results from ALCHEMIST may also benefit future lung cancer patients by helping scientists to:

• Screen for molecular features that may predict response to a drug with a given mechanism of action.

• Analyze tumor specimens at relapse to define mechanisms of resistance

Develop a public database that links clinical outcomes with molecular tumor characteristics.

ALCHEMIST is the second precision medicine clinical trial to launch as part of NCTN.

The first, Lung-MAP, for patients with advanced squamous cell lung cancer, launched in June (The Cancer Letter, June 20, Feb. 21).

NCTN and its impact on clinical trials will be discussed at the Sept. 9 meeting of the National Cancer Advisory Board.

## CAP Issues Active Surveillance Guidance for Prostate Cancer

The College of American Pathologists published recommendations for active surveillance of patients with prostate cancer.

The report highlighted key pathologic parameters for identifying patients likely to succeed with active surveillance, including: sampling, submission, and processing issues in needle biopsies; tumor extent in needle biopsies; biopsy reporting for all and special cases; Gleason scores; and precision medicine markers.

The recommendations were published online in the Archives of Pathology & Laboratory Medicine.

Recommendations from the U.S. Preventive Services Task Force and randomized trials have drawn attention to overtreatment of localized, low-risk prostate cancer. PSA screening and changing consensus on PSA testing practices are among the many factors that contribute to prostate cancer's overdiagnosis and overtreatment, according to CAP.

The article's authors include pathologists, radiation oncologists, surgeons, and urologists from Australia, Canada, Italy, New Zealand, Sweden, and the U.S. The recommendations were supported by the International Society of Urological Pathology, the Association of Directors of Anatomic and Surgical Pathology, the New Zealand Society of Pathologists, and the Prostate Cancer Foundation.



## Health Groups Urge FDA To Regulate Tobacco Products

The American Association for Cancer Research and the American Society of Clinical Oncology urged the FDA to regulate all tobacco products, including e-cigarettes.

Additionally, 24 public health and medical organizations filed public comments in response to an FDA proposal to extend its regulatory authority over tobacco products.

Specifically, AACR and ASCO called for banning youth-oriented advertising and marketing, self-service product displays, and tobacco company sponsorship of youth-oriented events, in addition to restricting sales to minors and implementing age-verification procedures for internet sales. All the organizations expressed concern about the proliferation of flavored e-cigarettes.

"We believe it is vitally important for the FDA to begin regulating these products, especially because we don't know much about the health effects of e-cigarette use," said ASCO President Peter Yu. "We are also quite concerned that e-cigarettes may increase the likelihood that nonsmokers or former smokers will use combustible tobacco products or that they will discourage smokers from quitting."

Roy Herbst, chair of the AACR Tobacco and Cancer Subcommittee, said, "There are insufficient data on the long-term health consequences of e-cigarettes, their value as tobacco cessation aids, or their effects on the use of conventional cigarettes," Herbst is chief of medical oncology at Yale Comprehensive Cancer Center. "Any benefits of e-cigarettes are most likely to be realized in a regulated environment in which appropriate safeguards can be implemented."

AACR and ASCO encouraged the agency to ban e-cigarette flavors or flavor names that are brand names of candy, cookies, soda, and other such products, and to prohibit e-cigarettes containing candy and other youth-friendly flavors, unless there is evidence demonstrating that they do not encourage young people to use these products.

"The proposed rule must be strengthened, and made comprehensive in scope, to prevent the manufacturers of tobacco products from designing and marketing their products in ways that undercut the full potential of the Tobacco Control Act to achieve its lifesaving objectives," the health groups wrote.

A recent study by the Centers for Disease Control and Prevention showed a three-fold increase in the number of youth using e-cigarettes who don't smoke

conventional cigarettes. The study also found that youth who have used e-cigarettes are twice as likely to have intentions of smoking conventional cigarettes.

"The finding that youth who have used an e-cigarette are twice as likely to express intent to smoke a traditional cigarette is an indication that the social norms our society have so carefully worked to achieve to reduce youth tobacco use and remove smoking from popular culture are being undermined," said Chris Hansen, president of the American Cancer Society Cancer Action Network.

"While the long-term health effects of using e-cigarettes are still unknown, we do know that when a child picks up an e-cigarette it can be the gateway to a life-long addiction to nicotine and exposure to the disease and death caused by tobacco products," he said.

The groups called for a final rule to be issued by April 25, 2015—one year after the proposal was officially published by the FDA. The agency currently regulates cigarettes, smokeless tobacco and roll-your-own tobacco under the 2009 Family Smoking Prevention and Tobacco Control Act.

AACR, ASCO, and the 24 other groups are all discouraging the FDA from exempting premium cigars from regulation, an option that is included in the proposed regulation.

"All cigars pose serious health risks," said Graham Warren, chair of ASCO's Tobacco Cessation and Control Subcommittee. "As the FDA itself noted in the proposed rule, even cigar smokers who do not inhale have a seven to 10 times higher overall risk of mouth and throat cancer compared with individuals who have never smoked. Exempting these dangerous products from FDA regulation is clearly not in the best interest of public health."

The health groups also point out that kids, and not just adults, smoke cigars, with a recent CDC survey showing that high school boys now smoke cigars at the same rate as cigarettes: 16.5 percent for cigars and 16.4 percent for cigarettes.

The 24 groups are: American Academy of Family Physicians, American Academy of Pediatrics, American Association for Respiratory Care, American Cancer Society Cancer Action Network, American College of Cardiology, American Congress of Obstetricians and Gynecologists, American Heart Association, American Lung Association, American Psychological Association, American Public Health Association, American Thoracic Society, Association of Maternal & Child Health Programs, Campaign for Tobacco-Free Kids, Cancer Prevention and Treatment Fund, Legacy, Lung Cancer Alliance, National African American Tobacco Prevention Network, National Association of City and County Health Officials, National Latino Alliance for Health Equity, Oncology Nursing Society, Partnership for Prevention, Prevention Partners, Society for Public Health Education, and Trust for America's Health.

*In Brief*

## Weiner to Begin Two-Year Term As President of AACI

(Continued from page 1)

Weiner is director of the Holden Comprehensive Cancer Center at the University of Iowa. He is also the C.E. Block Chair of Cancer Research, professor of internal medicine, and a faculty member in the Interdisciplinary Graduate Program in Immunology at the University of Iowa.

He will succeed current AACI President **Michelle Le Beau**, the Arthur and Marian Edelstein Professor of Medicine and director of the University of Chicago Comprehensive Cancer Center.

During her presidency, Le Beau launched the AACI's Molecular Diagnostics Initiative, which examines challenges impeding the implementation of comprehensive molecular diagnostics within cancer centers.

Weiner said that he would focus his AACI presidency on "the academic difference," the role academic cancer centers play in cancer patient care and research.

AACI also announced the election of **Stanton Gerson** as vice-president and president-elect.

Gerson is the Asa and Patricia Shiverick-Jane Shiverick (Tripp) Professor of Hematological Oncology, director of the Case Comprehensive Cancer Center, founding director of the National Center for Regenerative Medicine, and a distinguished university professor at Case Western Reserve University.

He is also director of University Hospitals Seidman Cancer Center and a member of the NCI Board of Scientific Advisors.

In a statement to AACI members, Gerson said he will prioritize three critical aspects of the nation's cancer centers program by: 1) encouraging the centers to work more closely together to lower health care costs and improve outcomes through nationally coordinated research and translation; 2) expanding the use of cancer patient data to further health improvements and research discoveries; and 3) making optimal use of the cancer center director and administrative leader network, including partnering with funding agencies, to

set the policy agenda for cancer research, dissemination of discoveries, and cancer health care.

Also elected to AACI's Board of Directors were **Patrick Loehrer, Sr.**, director of the Indiana University Melvin and Bren Simon Cancer Center, and **Thomas Sellers**, director and executive vice president of the Moffitt Cancer Center and Research Institute.

**THE EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY** named the winners of the society's annual awards, which will be presented Sept. 26 at the ESMO 2014 Congress in Madrid.

**Carsten Bokemeyer** will receive the ESMO Award for his commitment to accelerate the transition of cancer discovery into real benefit for patients.

Bokemeyer is director of the University Cancer Center Hamburg, one of Germany's oncology centers of excellence. Bokemeyer's discoveries include identifying the early stages of malignant germ cell transformation and the mechanisms of resistance of these tumors to chemotherapy. He has also developed new therapeutic concepts with cytostatic drugs and immunotherapy in solid tumors.

**Peter Boyle** will receive the ESMO Lifetime Achievement Award for his long-standing contribution to cancer epidemiology, education and prevention.

Boyle is a professor of global public health at the University of Strathclyde, a visiting professor at the University of Glasgow and an honorary professor at Yale University. He is also founder and president of the World Prevention Alliance. He led the EUROCAN+PLUS project for the European Parliament to develop priorities for cancer research in Europe and was editor of the World Cancer Report 2008 and the State of Oncology 2013.

**Heikki Joensuu** will receive the Hamilton Fairley Award for his contributions to improve breast cancer and GIST diagnostics and care.

In 2000, Joensuu discovered that imatinib was effective for most advanced GIST and in 2011 found that as adjuvant treatment it improved recurrence-free survival and possibly overall survival. Joensuu became professor of oncology at the age of 37 and is currently academy professor at the University of Helsinki and research director at the Helsinki Comprehensive Cancer Centre.

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**CHARLES LEMAISTRE** and **HANS MARK** were named chancellors emeriti of the **University of Texas System** Board of Regents.

LeMaistre served as the fourth UT System chancellor, from 1971 to 1978, while the UT System expanded to include health science centers in Houston and San Antonio, and new universities in Dallas, Permian Basin and San Antonio. LeMaistre then served as the third president of MD Anderson Cancer Center.

LeMaistre devoted much of his professional career to cancer prevention and smoking control. He served on the first U.S. Surgeon General's Advisory Committee on Smoking and Health in 1964, and later as the national president of the American Cancer Society.

He was president of MD Anderson from 1978 to 1996, during which time the institution doubled in size. He helped establish the center's cancer prevention program, and today serves as president emeritus.

Among his awards and recognitions, LeMaistre received the President's Award from the American Lung Association in 1987 and the Distinguished Service Award from the American Medical Association in 1995.

Mark is a physicist and retired professor of aerospace engineering who served as the sixth chancellor of the system, from 1984 to 1992. He played a prominent role in bringing the high-tech industry to Austin and Central Texas, including the Microelectronics and Computer Technology Corporation and Semiconductor Manufacturing Technology.

Mark had served as deputy administrator of NASA, where he assisted in developing the space station and oversaw 14 space shuttle flights. He taught at several universities, including MIT, UC Berkeley and Stanford, and he also served as Secretary of the U.S. Air Force.

He has received a number of awards and accolades, including the Distinguished Service Medal from NASA and the U.S. Navy's Distinguished Public Service Award, the highest civilian honor, for his more than 50 years of military research. He is a fellow of the American Institute of Aeronautics and Astronautics and the American Society of Engineering Education, among others.

Mark retired recently as the John J. McKetta Centennial Energy Chair in Engineering at UT Austin after teaching there for 23 years.

Only two other chancellors, Harry Huntt Ransom and E. Don Walker, have been named chancellor emeritus.

**JAMES DAVIS** was elected chairman of the **The Leukemia & Lymphoma Society**.

Davis, who will serve a two year term as chair, is a chronic myeloid leukemia patient and clinical trial

participant. He has served in several capacities with LLS, starting in 2007, including vice-chair of the board of directors, chair of the mission oversight committee, and as a member of the Therapy Acceleration Program medical & scientific affairs and executive committees.

Davis has also served for two years as the co-chair of the National Capital Area chapter's annual Leukemia Ball, helping to raise approximately $6 million.

Davis is the former executive vice president, general counsel and secretary of Human Genome Sciences Inc.

**JOYCE WONG** was named the 2014 Certified Pediatric Oncology Nurse of the Year by the **Oncology Nursing Certification Corporation**.

Wong is the integrative services coordinator at Kapiolani Medical Center for Women and Children.

She was in the first group of certified nurses at her institution, and actively encourages and mentors other nurses to become certified. Wong is a strong proponent of holistic care, and she leads the complementary medicine program at Kapiolani. She became certified in Healing Touch in 2000, and later also became a licensed massage therapist.

**PATRICK SOON-SHIONG** was named global director for cancer services and bioinformatics of **Providence Health & Services**.

A partnership was also announced: Soon-Shiong, through his Chan Soon-Shiong Institute of Molecular Medicine, and Providence will create a clinical genomic network for whole genomic sequencing. They will use an Illumina HiSeq X Ten sequencing system to establish the first CLIA-approved clinical facility to drive molecular decisions for cancer patients.

Providence will be the first health care system to use the sequencing system. The HiSeq X Ten is the first platform to deliver population-scale whole genome sequencing, and is capable of sequencing thousands of samples annually.

Soon-Shiong is the founder and CEO of NantHealth. He has led the development of a system that can analyze genetic data from a tumor sample in 47 seconds and transfer the data in 18 seconds. He is also a professor of microbiology, immunology, molecular genetics and bioengineering at the University of California Los Angeles.

**SHAWN CLINE TOMASELLO** was appointed chief commercial officer of **Pharmacyclics Inc.**

Cline Tomasello is former president of the Americas, hematology and oncology, for the Celgene Corporation. Prior to joining Celgene, she served as the national director of hematology for Rituxan at Genentech.

**JEFFREY LITWIN** was named editor-in-chief of the **Journal of Clinical Trial Results.**

The online, open-access, peer-reviewed publication serves researchers, clinicians, and other professionals, and is expected to launch in 2015.

Litwin, a board-certified cardiologist and internist, is president and CEO of ERT, which provides patient safety and efficacy endpoint data collection solutions and technology services.

"Although many journals focus on positive results from high-profile trials, data from all clinical studies remain valuable contributions to the medical literature," said Litwin. The sharing of trials that have not resulted in a successful outcome is rare, and by publishing this information, the Journal of Clinical Trial Results will make a great contribution to our knowledge base."

**MD ANDERSON CANCER CENTER** and **Memorial Hermann Health System** formed a partnership to provide specialized breast screening at a network of community breast care centers in the greater Houston area.

Beginning in late November, MD Anderson will become the exclusive provider of professional breast radiology services for five of Memorial Hermann's 10 breast care centers, located in Memorial City, The Woodlands, Northeast, Southwest and Sugar Land.

Over time, the network will expand to Memorial Hermann's locations in Katy, Pearland, Pasadena, Upper Kirby and Northwest. In addition, expansion planning is underway for centers in Cypress, South Katy and Spring.

Under the agreement, the breast screening network will offer screening and diagnostic services, utilizing existing Memorial Hermann facilities and technical resources, including equipment and staff. MD Anderson's radiologists will interpret the screening or diagnostic images, perform biopsies if needed, and consult with patients and physicians.

**THE LIVESTRONG FOUNDATION** announced that it will launch the **LIVESTRONG Cancer Institutes** to create an original model of patient-centered cancer care, in partnership with the **Dell Medical School at The University of Texas**.

The cancer institutes, which will be funded by an investment of $50 million over 10 years from the foundation, will be designed by cancer patients and survivors to deliver patient-centered care. The two organizations will work over the coming months to agree upon milestones and elements of service and establish replicable models of care.

**MD ANDERSON CANCER CENTER** opened a full-service diagnostic imaging center in West Houston.

General imaging services available at the center include Magnetic Resonance Imaging, computed tomography, positron emission tomography, general and Doppler ultrasound for diagnostics and biopsies, and digital X-ray.

Located in a separate women's imaging center are ultrasound, 3D digital breast tomosynthesis, ultrasound-guided biopsies and other technologies that will allow radiologists and staff to return a same-day diagnosis. Digital mammography for screening and diagnostics also is available.

*Drug Approvals*

## Accelerated Approval Granted To Keytruda Antibody In Metastatic Melanoma

**FDA granted accelerated approval for Keytruda (pembrolizumab)** for unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.

The indication was approved based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Keytruda received a Breakthrough Therapy designation for advanced melanoma, and is the first anti-programmed death receptor-1 therapy approved in the U.S.

The designation was granted based on the significance of early study findings and the unmet medical need. For the recommended 2 mg/kg dose based on data in 89 patients, the overall response rate was 24 percent (95% CI: 15, 34), with one complete response and 20 partial responses (21/89). At the time of analysis, 86 percent (18/21) of patients with objective responses had ongoing responses with durations ranging from 1.4+ to 8.5+ months, including eight patients with ongoing responses of 6 months or longer. Fourteen percent (3/21) had progression of disease 2.8, 2.9, and 8.2 months after initial response.

Keytruda is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, and may affect both tumor cells and healthy cells. Immune-mediated adverse reactions occurred with Keytruda including pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hyperthyroidism, and hypothyroidism.

Merck, the drug's sponsor, is conducting ongoing phase II and III clinical studies in advanced melanoma.

**FDA approved Cologuard**, the first stool-based colorectal screening test that detects the presence of red blood cells and DNA mutations that may indicate the presence of certain kinds of abnormal growths that may be cancers such as colon cancer or precursors to cancer.

Using a stool sample, Cologuard detects hemoglobin and certain mutations associated with colorectal cancer in the DNA of cells shed by advanced adenomas as stool moves through the large intestine and rectum. Patients with positive test results are advised to undergo a diagnostic colonoscopy.

The Centers for Disease Control and Prevention estimate that if everyone age 50 or older had regular screening tests as recommended, at least 60 percent of colorectal cancer deaths could be avoided.

"This approval offers patients and physicians another option to screen for colorectal cancer," said Alberto Gutierrez, director of the Office of In Vitro Diagnostics and Radiological Health at the FDA's Center for Devices and Radiological Health. "Fecal blood testing is a well-established screening tool and the clinical data showed that the test detected more cancers than a commonly used fecal occult test."

This approval does not change current practice guidelines for colorectal cancer screening. Stool DNA testing is not currently recommended as a method to screen for colorectal cancer by the U.S. Preventive Services Task Force. Among other guidelines, the USPSTF recommends adults age 50 to 75, at average risk for colon cancer, be screened using fecal occult blood testing, sigmoidoscopy or colonoscopy.

The safety and effectiveness of Cologuard was established in a clinical trial that screened 10,023 subjects. The trial compared the performance of Cologuard to the fecal immunochemical test, a non-

invasive screening test that detects blood in the stool.

Cologuard accurately detected cancers and advanced adenomas more often than FIT, detecting 92 percent of colorectal cancers and 42 percent of advanced adenomas in the study population, while FIT screening detected 74 percent of cancers and 24 percent of advanced adenomas.

Cologuard was less accurate than FIT at correctly identifying subjects negative for colorectal cancer or advanced adenomas. Cologuard correctly gave a negative screening result for 87 percent of the study subjects, while FIT provided accurate negative screening results for 95 percent of the study population, according to Cologuard's sponsor, Exact Sciences.

**The Centers for Medicare & Medicaid Services issued a proposed national coverage determination for Cologuard**. Cologuard is the first product reviewed through a joint FDA-CMS pilot program known as parallel review where the agencies concurrently review medical devices to help reduce the time between the FDA's approval of a device and Medicare coverage.

This voluntary pilot program is open to certain premarket approval applications for devices with new technologies and to medical devices that fall within the scope of a Part A or Part B Medicare benefit category and have not been subject to a national coverage determination.

"Parallel review allows the last part of the FDA process to run at the same time as the CMS process, cutting as many as six months from the time from study initiation to coverage," said Nancy Stade, CDRH's deputy director for policy. "The pilot program is ongoing, but we will apply what we have learned to improve the efficiency of the medical device approval pathway for devices that address an important public health need."

"This is the first time in history that FDA has approved a technology and CMS has proposed national coverage on the same day," said Patrick Conway, chief medical officer and deputy administrator for innovation and quality for CMS. "This parallel review represents unprecedented collaboration between the two agencies and industry and most importantly will provide timely access for Medicare beneficiaries to an innovative screening test to help in the early detection of colorectal cancer."

CMS proposes to cover the Cologuard test once every three years for Medicare beneficiaries who meet all of the following criteria: age 50 to 85 years; asymptomatic, including but not limited to lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test; and an average risk of developing colorectal cancer, including no personal history of adenomatous polyps, of colorectal cancer, or inflammatory bowel disease, including Crohn's Disease and ulcerative colitis.

**FDA approved a new use for Avastin (bevacizumab)** to treat patients with persistent, recurrent or late-stage cervical cancer. The new indication is approved for use in combination with paclitaxel and cisplatin or in combination with paclitaxel and topotecan.

"Avastin is the first drug approved for patients with late-stage cervical cancer since the 2006 approval of topotecan with cisplatin," said Richard Pazdur, director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "It is also the first biologic agent approved for patients with late-stage cervical cancer and was approved in less than four months under the FDA's priority review program."

Avastin interferes with the blood vessels that fuel the development of cancerous cells. Avastin is also approved in the U.S. to treat cancers of the colon, kidney, and lung. The approval in advanced cervical cancer was based on the GOG-0240 study, which enrolled 452 participants with persistent, recurrent, or late-stage disease.

Participants were randomly assigned to receive paclitaxel and cisplatin with or without Avastin or paclitaxel and topotecan with or without Avastin. Results showed an increase in overall survival to 16.8 months in participants who received chemotherapy in combination with Avastin as compared to 12.9 months for those receiving chemotherapy alone.

GOG-0240 is an independent, NCI-sponsored study of the Gynecologic Oncology Group. Avastin is marketed by Genentech, a member of the Roche Group.

**Health Canada approved Abraxane for Injectable Suspension** for first-line treatment of adult patients with metastatic pancreatic cancer, representing the first approved treatment for this disease in nearly two decades.

Approval of Abraxane (paclitaxel powder for injectable suspension; nanoparticle, albumin-bound paclitaxel) was based on the results of MPACT, an open-label, phase III, randomized, international study which was published in the New England Journal of Medicine in October 2013.

The study involved 861 chemotherapy-naïve

patients with metastatic pancreatic cancer from 11 countries, including Canada, and showed a statistically significant improvement in median overall survival with Abraxane plus gemcitabine compared to gemcitabine alone: 8.5 vs. 6.7 months, respectively (HR 0.72, P<0.0001); a 28 percent overall reduction in risk of death.

"It's been quite some time since we've seen any type of treatment advance for pancreatic cancer making this news so important for patients." said Laurie Ellies, co-founder and acting executive director of Pancreatic Cancer Canada. "Over the past decade, there has been a significant improvement in cancer survival rates. Sadly, the same cannot be said about pancreatic cancer.

"This year alone, we can expect an estimated 4,700 Canadians will be diagnosed with this disease."

Abraxane is formulated with albumin, a human protein, and is free of solvents. Abraxane in combination with gemcitabine for the treatment of metastatic pancreatic cancer is approved in the U.S. and 30 other countries.

**The European Medicines Agency approved Eisai's request for accelerated assessment of lenvatinib** for the treatment of patients with progressive radioiodine-refractory differentiated thyroid cancer.

Lenvatinib is an oral multiple receptor tyrosine kinase inhibitor with a novel binding mode that selectively inhibits the kinase activities of vascular endothelial growth factor receptors, in addition to other proangiogenic and oncogenic pathway-related RTKs, including fibroblast growth factor receptors, the platelet-derived growth factor receptor PDGFRalpha, KIT, and RET.

Lenvatinib received orphan drug designation for the treatment of follicular and papillary thyroid cancer from the European Commission in April 2013.

The EU marketing authorization application will be based on the results of the Phase III SELECT trial of lenvatinib that demonstrated extended progression free survival compared to placebo (HR=0.21, [99% CI, 0.14-0.31]; p<0.0001). The median lengths of PFS of lenvatinib and placebo were 18.3 and 3.6 months, respectively.

Secondary endpoints of the study included overall response rate, overall survival and safety. The study enrolled 392 patients in over 100 sites in Europe, North and South America and Asia and was conducted by Eisai in collaboration with the SFJ Pharmaceuticals Group. Eisai expects to file for lenvatinib in the next few months.

*Obituaries*

## Jessie Gruman, 60, CFAH Founder and President

Jessie Gruman, founder and president of the Center for Advancing Health since 1992, died July 14. She was 60.

Gruman advocated for policies and practices based on her own experiences of treatment for five cancer diagnoses, interviews with patients and caregivers, surveys and peer-reviewed research. She had five cancers, starting with Hodgkin's lymphoma at age 20, followed by cancers of the cervix, colon, and stomach. At 59, she received the diagnosis of metastatic lung cancer.

She was the author of AfterShock: What to Do When the Doctor Gives You – or Someone You Love – a Devastating Diagnosis; Slow Leaks: Missed Opportunities to Encourage Our Engagement in Our Health Care; A Year of Living Sickishly: A Patient Reflects; The Experience of the American Patient: Risk, Trust and Choice; Behavior Matters; as well as scientific papers, opinion essays and articles.

"The Center has lost a brilliant colleague," said M. Chris Gibbons, chair of the board of trustees of the Center for Advancing Health. "Those of us who have been fortunate enough to know and work with Jessie have lost a dear friend."

"Jessie was a tireless advocate for patients. For the past ten years, Jessie focused her efforts and the efforts of CFAH on advancing patient engagement as well as helping people find and benefit from good health care," he said. "We will deeply miss her powerful and inspiring voice for patients, families and caregivers."

Gruman was a member of the American Academy of Arts and Sciences and the Council on Foreign Relations and was a fellow of the New York Academy of Medicine and the Society for Behavioral Medicine.

She received honorary doctorates from Brown University, Carnegie Mellon University, Clark University, Georgetown University, New York University, Northeastern University, Salve Regina University, Syracuse University and Tulane University, and the Presidential Medal of the George Washington University.

She was also honored by Research!America, the National Coalition for Cancer Survivorship, and the Society for Behavioral Medicine, which in 2014 created the Jessie Gruman Award for Health

Engagement to recognize annually an individual who has made a pivotal contribution to research, practice or policy in the field of health engagement.

Gruman received a B.A. from Vassar College and a Ph.D. in Social Psychology from Columbia University and was a professorial lecturer in the School of Public Health and Health Services at the George Washington University.

Gruman worked at NCI, the American Cancer Society and AT&T.

Memorial services will be held in October in New York and Washington, D.C. CFAH has been collecting published tributes to Gruman on its Prepared Patient Blog, to which she often contributed.

## Jesse Leonard Steinfeld, 87, Former U.S. Surgeon General

Jesse Leonard Steinfeld, U.S. surgeon general from 1969 to 1973, died Aug. 5. He was 87.

He had served as deputy director of NCI and deputy assistant secretary for Health and Scientific Affairs before being appointed surgeon general by President Richard Nixon.

Steinfeld began his tenure as surgeon general at a time when smoking was starting to become a major issue of public health. The first definitive, causal link between smoking and lung cancer was reported in 1964 in the landmark publication of the Surgeon General's Report on Smoking and Health, issued by his predecessor Luther Terry, which received widespread media coverage and marked the beginning of a significant shift in public attitudes about smoking.

Cigarette packs began carrying caution labels in 1965, alerting consumers that "cigarette smoking may be hazardous to your health." In 1970, while Steinfeld was acting surgeon general, the labels began to carry a bolder warning: "The surgeon general has determined that cigarette smoking is dangerous to your health."

Voicing his concerns over studies that found women were less likely than men to quit smoking, Steinfeld spoke out against the tobacco industry's marketing toward women, and led a campaign to warn them that smoking is harmful not only to their own health, but that of their children and unborn fetuses. Additionally, he stressed the negative effects smoking had on one's appearance, such as wrinkles and poor teeth.

Steinfeld graduated from the University of Pittsburgh in 1945, 19 months after finishing high school at the age of 16. He received his medical degree from what is now Case Western Reserve University, in 1949, at the age of 22. Steinfeld completed an internship at what is now Cedars-Sinai Hospital in Los Angeles and residencies at the Veterans Affairs Hospital in Long Beach, California, and the Laboratory of Experimental Oncology at the University of California, San Francisco Hospital.

Steinfeld had also served on the faculties of UCSF; George Washington University School of Medicine; and the University of Southern California School of Medicine. He also served as physician aboard a Coast Guard ship in the North Atlantic during the Korean War.

Steinfeld also served as president of the American Society of Clinical Oncology from 1970 to 1971.

According to ASCO, before Nixon's January 1971 State of the Union address, Steinfeld suggested that the budget of the NCI be increased from $200 million to $300 million. In December 1971, Nixon signed the National Cancer Act.

Steinfeld offered his resignation as surgeon general in 1972 and stepped down from the position at the end of January 1973.

He was an antitobacco crusader—and was named the "worst surgeon general ever" by the tobacco industry, according to the American Association for Cancer Research. He had been a member of the AACR since 1956.

In an interview years later, he said he felt he was not able to keep his position because of his antismoking work. The surgeon general's office was not filled again until President Jimmy Carter appointed Julius Richmond in 1977.

He went on to serve as director of the Mayo Clinic Comprehensive Cancer Center and professor of medicine at the Mayo Medical School; professor of medicine at the University of California, Irvine and chief of medicine at the Veterans Affairs Hospital in Long Beach; dean and professor of medicine at the Medical College of Virginia in Richmond; and president of the Medical College of Georgia in Augusta, a position he held until he retired in 1987.

He is survived by his wife, three daughters, and two grandchildren.