THE CANCER LETTER

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J&J Withdraws Power Morcellators, Citing Risk of Disseminating Cancer

By Matthew Bin Han Ong

Ethicon, the Johnson & Johnson subsidiary that manufactures nearly three-quarters of laparoscopic power morcellators on the market, has requested a withdrawal of the controversial devices.

"Immediately review inventory to determine if you have any Ethicon Morcellation Devices which are the subject of this market withdrawal," the company wrote in a letter to hospitals worldwide.

"If you have provided Ethicon Morcellation Devices to any hospital within your system, you are responsible for notifying the appropriate parties immediately," said the letter dated July 31.

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FDA Moves to Regulate Lab-Developed Tests

By Paul Goldberg

FDA announced two plans to resolve a cluster of impediments to personalized cancer care:

• Targeted drugs will need to be approved simultaneously with companion diagnostics that would determine who should—and shouldn't—get the drug.

• At the same time, the agency will begin phasing in oversight of the essentially unregulated terrain of "laboratory-developed tests."

Tests that are intended to select therapy for deadly diseases including cancer would be among the first to be subjected to regulation.

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In Brief

IOM Cancer Forum Appoints Six Members

THE NATIONAL CANCER POLICY FORUM, an advisory group of the Institute of Medicine, appointed six at-large members.

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Hospitals to Return Morcellators For Refunds from Manufacturer

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Ethicon said it will reimburse customers for all devices returned by Dec. 30, 2014.

The company's decision to pull the devices off the market comes as a result of a series of extraordinary events:

• Eight months ago, two Harvard physicians launched a high-profile campaign against power morcellation (The Cancer Letter, July 4).

• Three months ago, FDA issued in an advisory on power morcellation, a move that was soon followed by Ethicon's decision to suspend global sales of the devices.

• Three weeks ago, several members of an FDA advisory panel expressed low confidence in power morcellation as a treatment for uterine fibroids (The Cancer Letter, July 25).

• Last week, a study in JAMA said that one in 368 women undergoing hysterectomies have an undetected uterine cancer that could be spread by a power morcellator's spinning blades.

The two Harvard physicians—Amy Reed and Hooman Noorchashm—said they were inundated by emails and phone calls when word of the withdrawal got out Wednesday evening.

"Everyone saw this as a victory," said Amy Reed, the anesthesiologist at Beth Israel Deaconess Medical Center who had her undetected leiomyosarcoma disseminated by the procedure in October 2013.

"I still think we have a long way to go with the whole morcellator business, further to go with the legislation that led to this, and potentially even further to change the thinking of the specialty.

"But the overwhelming opinion of everyone was, 'We won.'"

Ethicon officials said the decision to withdraw the device is based on an "uncertain" risk-benefit assessment of hysterectomy and myomectomy procedures performed with power morcellators.

Morcellation has been a standard practice in gynecology for nearly two decades. Power morcellators, which typically cost $1,500 to $3,000 per unit, have been used on an estimated 100,000 women a year in the U.S.

"Due to this continued uncertainty, Ethicon believes that a market withdrawal of Ethicon morcellation devices is the appropriate course of action at this time until further medical guidelines are established and/or new technologies are developed to mitigate the risk," Ethicon said in a statement. "We remain committed to advancing the standard of care for women's health and will continue to monitor and evaluate this important issue."

Johnson & Johnson held an estimated 72 percent of the market share for power morcellators in 2011, according to iData Research Inc., a market research firm.

A voluntary withdrawal initiative is the strongest action Ethicon can muster, said Thomas Greene, a civil litigation attorney who has represented Reed and Noorchashm.

"Manufacturer-initiated recalls are voluntary recalls," Greene said to The Cancer Letter. "This is not a half-measure by Johnson & Johnson—this is the company taking the strongest action it can to limit future use of its power morcellators. And it's important to note that so-called 'voluntary' recalls don't mean Johnson & Johnson cannot take other kinds of action, like sending employees to retrieve the devices.

"Only the FDA can issue a mandatory recall. The movement to ban use of power morcellators in this context has been picking up a lot of steam recently, but the FDA has not yet acted on its own to prevent the upstaging of cancer in patients through the use of power morcellators."

The withdrawal is a sign that Johnson & Johnson recognizes the harm their devices can cause, Greene said.

"The company has made a decision that is in its own best interest to prevent future use of its power morcellators to the extent it can," he said. "Johnson & Johnson knows that their products cannot be used safely to morcellate uterine fibroids, because there is no definitive test to determine if fibroids are benign or cancerous."

The move will limit the company's future liability, Greene said.

"I think the company understands now that it is not blameless for its role in promoting the use of

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morcellators despite mounting evidence of cancer deaths," he said. "The recall will have the effect of capping their liability to claims that arise from the use of power morcellators that are not returned."

Hospitals, OBGYN Groups Respond

The Allegheny Health Network, a large hospital system with 250 facilities throughout Pennsylvania, promptly responded to the withdrawal announcement.

"[The morcellators] have already been sent back," a spokesperson for the network said to The Cancer Letter. "Allegheny Health Network follows the FDA's recommendations, as well as those of the leading OBGYN and gynecologic oncology professional organizations, and has carefully weighed the benefits and risks of power morcellation for fibroid removal on an individual patient basis.

"We will continue to abide by the recommendations of these groups and will comply with any recall of devices that we are using. Power morcellation is offered only when a closed collection system is used to limit the spread of tissue during hysterectomy or fibroid removal. Allegheny Health Network does not offer the procedure without this safeguard and each patient is counseled on risks, benefits and alternatives to the procedure."

Other institutions, including the University of Pittsburgh Medical Center, are evaluating their position on the issue.

"As noted previously in May, UPMC immediately adopted changes in our practice, significantly reducing the use of morcellators for hysterectomy and uterine fibroid removal," officials said in a statement to The Cancer Letter. "In addition, we are now requiring those physicians still using morcellators to use a containment bag, significantly reducing exposure to any undetected cancerous cells.

"UPMC is currently reevaluating our position based on the Johnson & Johnson announcement."

The American College of Obstetricians and Gynecologists called the withdrawal "unfortunate."

"Our position hasn't changed," an ACOG spokesperson said to The Cancer Letter. "And our position is based on science."

ACOG officials stressed the importance of informed consent as a way to improve the use of morcellation—a position opposed by several members of the FDA Obstetrics and Gynecology Devices Advisory Committee, who said informed consent protects the practitioner from liability, not the patient.

"Unfortunately, the impact of today's withdrawal of some morcellators from the market will be felt most strongly by America's women," ACOG said in a statement. "While there is a potential risk associated with morcellation, there is also a significant benefit associated with avoiding total abdominal hysterectomy and its increased risk of infection, bleeding, bowel injury, blood clots and death. In other words, there is significant risk on both sides and benefit on both sides.

"We hope that, moving forward, women will continue to speak with their physicians about their treatment options, which can include laparotomy, total abdominal hysterectomy, and vaginal hysterectomy, which we have previously recommended because it is associated with better outcomes and fewer complications."

The American Association of Gynecologic Laparoscopists similarly called for further validation of evidence.

"At present, there exists no new valid scientific information to change the position statement of the AAGL," said Jubilee Brown, an associate professor at MD Anderson Cancer Center and a member of AAGL's board of trustees. "The AAGL's policies are based on scientific merit and on full evaluation of the beneficial impact of minimally invasive surgery for patients worldwide. We will continue to support evidence-based medicine and comprehensive consideration of the risks and benefits of each surgical procedure.

"The AAGL recognizes that information continues to be produced," said Brown, director of gynecologic oncology at The Women's Hospital of Texas, and associate professor in the Department of Gynecology Oncology and Reproductive Medicine at MD Anderson. "Scientific papers including the recent JAMA study, the upcoming study by Pritts et al., the study by Naumann et al., and certainly additional future publications will continue to inform the decision-making surrounding this issue. The AAGL and its Task Force on Tissue Extraction Techniques will continue to evaluate these data in a dynamic fashion, and we will amend our stance and policies as the scientific data warrant."

Brown said AAGL recognizes that the withdrawal request is within the scope of Ethicon's business policy—a decision that will impact many gynecologists.

"The withdrawal of power morcellators by Ethicon will certainly limit the ability of many gynecologists to offer power morcellation as a treatment option to their patients with large fibroids," she said. "This may result in an increase in open laparotomies for the treatment of benign fibroids."

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Reed: "The Beginning of the End"

Ethicon's withdrawal of its power morcellators is the turning point in the narrative, Reed said.

"We're encouraged by this," she said to The Cancer Letter. "We were encouraged after the FDA panel had gotten together, but still—there is always room for doubt that they would come out definitively.

"However, I feel like this is the first step to really putting an end to this.

"I'm happy that other women will be spared what I went through, but part of me is still angry it's been going on for two decades, and it happened to us, and we had to sacrifice. Especially my husband—professionally and personally—we had to sacrifice to get it to come to this. To me and to so many people, I think this is so obvious, that the fact that it has taken two decades, it's kind of bittersweet.

It's notable that it was a device manufacturer who took this decisive step toward resolution of the controversy, Reed said. Physicians and their associations should have been at the forefront of demanding changes, but—disappointingly—were not, she said.

"My husband and I are both physicians, and the last thing that we want is to have regulatory bodies made up of non-physicians telling us how we practice, or telling us what's the right thing to do for patients, because that's all we do," she said. "But the fact that the gynecologic community has been so unable to self-regulate when it comes to this, it's crazy.

"You think that the doctors do what's best for the patients, and businesses do what's best for their business, but here you have a case where doctors are not doing what's best for the patients, and the businesses are actually saying, 'You know what, we're pulling these off the market because this is not what's best for patient care.'

"I'm sure all of that is financially motivated, but still, the fact that physicians are pushing for this procedure to remain in practice when the government is saying this is not a good idea—soon it's going to become clear how wrong they are in that stance.

"I have to imagine that people within the gynecology community are shifting, and it's only those last vocal people that are making the headlines. But overall, it's disheartening because we are becoming so entrenched in our specialty—that Hippocratic oath that we take is designed to prevent things like this from happening."

Sponsors of Targeted Drugs Calling for Regulation of LDTs

(Continued from page 1)

The two actions are interconnected, FDA officials said during a press call July 31.

"The first category [of tests to receive scrutiny by FDA] will be those LDTs for the same intended use of a companion diagnostic we've already approved, because at that point you already have a companion diagnostic you know is accurate and reliable to use for directing use for that particular drug," Jeffrey Shuren, director of the FDA's Center for Devices and Radiological Health, said at the press call.

Pharmaceutical companies that develop targeted agents have been asking the agency to regulate LDTs for years. However, the agency has been exercising "enforcement discretion," staying away from requiring validation of such tests.

Now, the boundaries of enforcement discretion will tighten, based on risk posed by the devices in question.

The agency took the following actions:

• It issued a final guidance on the development, review and approval or clearance of companion diagnostics. These tests are commonly used to detect certain types of gene-based cancers.

• It notified Congress of its intention to publish a draft guidance outlining a risk-based framework for oversight of laboratory developed tests.

FDA plans to release a draft guidance in about two months. The agency estimates that there are currently around 11,000 LDTs developed by about 2,000 labs in the U.S.

The first wave of the tests offered by these labs would become subject to review within a year after the framework becomes final, and the final wave will come through within nine years.

The notice to Congress is required under the Food and Drug Administration Safety and Innovation Act of 2012. The agency has to notify Congress 60 days before issuing guidance or any regulation that may affect LDTs.

The agency already oversees direct-to-consumer tests regardless of whether they are LDTs or traditional diagnostics.

"Ensuring that doctors and patients have access to safe, accurate and reliable diagnostic tests to help guide treatment decisions is a priority for the FDA," said FDA Commissioner Margaret Hamburg. "Inaccurate test results could cause patients to seek unnecessary treatment or delay and sometimes forgo treatment altogether. Today's action demonstrates the agency's

commitment to personalized medicine, which depends on accurate and reliable tests to get the right treatment to the right patient."

FDA Actions Aim to Solve Related Problems

During the press call, Shuren said the issues at the heart of the two regulatory actions are inseparable.

Asked whether pharmaceutical companies are objecting to the mandate of identifying test kits as a condition of approval of targeted drugs, Shuren said the agency hasn't run into any such opposition.

To begin with, pharma companies have likely identified appropriate diagnostic tests at the time they conduct clinical trials, Shuren said.

"For a companion diagnostic, for the drug to truly be safe and effective depends upon having an accurate and reliable test available," he said. "So they really are bound up with one another.

"In fact, in our reviews to date, there has been no holdup in terms of a decision on a therapeutic because of a diagnostic review. We have reviewed those companion diagnostics in the same timeframe as the drug developers.

"But from the developers, the thing we hear most is the fact that we are not regulating the LDTs.

"So, we've had a company that goes out there, they have a therapeutic we approved, they have a companion diagnostic we approved, and on the very same day a whole bunch of labs come up and say, 'Oh, guess what, we make the same test, and not only that, our test is better." And there is no way to know that.

"The company did all the studies, they have the data, and they are complaining: 'Why are we investing to make this therapeutic to help patients? Why bother to develop a diagnostic test, when the labs can go ahead and throw something out there and compete, and they don't have to do anything to show that?

"And so they are coming to us, saying 'We are not thinking to invest the same way.' What we are trying to do in the framework is balance these particular concerns."

The Washington, D.C., lobby for LDTs, the American Clinical Laboratory Association, said the agency's plans to start regulating such tests would "stifle diagnostic innovation and ultimately jeopardize patient access to timely and effective treatments."

"Laboratories have been regulated for decades by the Centers for Medicare and Medicaid Services under the Clinical Laboratory Improvement Amendments and by state law," Alan Mertz, president of ACLA, said in a statement. "Under the CLIA framework, a thorough and detailed regulatory process, we've seen an explosion of innovation in laboratory diagnostics.

"To the extent that stakeholders have concerns about possible regulatory gaps under CLIA, ACLA has long supported enhancing the CLIA regulatory framework, rather than impose an additional layer of regulation based upon a different statute designed for manufactured products rather than laboratory testing."

History of Enforcement Discretion

Shuren said FDA is moving toward regulation because "the world has changed."

"Back when we were first implementing the program in 1976, these were relatively simple tests that were being used by the local labs for the local patient populations, to meet their needs—and a lot of times for rare diseases," he said. "When we were setting up the program, we focused our resources on the other kinds of devices.

"But in the interim things have changed. We have seen increasingly more risky LDTs out on the market. There are reports now of faulty LDTs that led to misdiagnosis, lead to failure to treat, or wrong treatment for patients. And we are now seeing these tests being made available to a nationwide audience, and all of that increases the risk to patients.

"What we are not proposing is to regulate them all the same. We will apply a risk-based approach and focus our attention where the risk to patients is the greatest, and strike that balance between assuring that the tests are safe and effective tests, where doctors and patients can be assured the results are accurate and reliable, and at the same time still try to facilitate innovation and development of new tests to meet patients' and practitioners' needs."

The agency will make exceptions for some devices.

Asked to describe the validation that would be required, Katie Serrano, deputy director of the FDA Division of Chemistry and Toxicology Devices, said de novo tests may not be required.

"We would be looking for evidence that the test can meet its intended use," Serrano said at the press call. "Clinical data would likely be a part of that premarket submission. It wouldn't necessarily have to come from the clinical studies that they had performed. It could also rely on data that have already been published."

The guidance will also make exceptions. These will include tests used for forensic purposes and those used in CLIA-certified, high-complexity histocompatibility laboratories for transplantation.

Also, the humanitarian use devices exemption would apply. A device may qualify this designation

when the number of persons who may be tested with the device is fewer than 4,000 per year.

NIH Director Francis Collins applauded the FDA's actions.

"This is good news for all who are working to turn the dream of personalized medicine into a reality," he said in a statement. "NIH supports our sister agency's proposal and thinks that this thoughtful framework—which focuses greatest attention on tests with the most significant clinical impact—will protect public health, without putting a damper on biomedical innovation or placing an undue burden on industry."

The American Association for Cancer Research also came out in support of the framework.

"The recent announcements by the FDA are aimed at providing patients and their physicians with an important level of confidence and certainty with regard to the highly complex molecular and genetic information that these diagnostic tests are determining," said Carlos Arteaga, AACR president, and professor of medicine and cancer biology and associate director for clinical research at the Vanderbilt-Ingram Cancer Center of Vanderbilt University.

"In addition, these actions by the FDA will serve as a catalyst for incentivizing innovation, which is vital during this time of unprecedented scientific opportunity.

"As an organization that represents the entire continuum of research, from the laboratory to the clinic, including the clinical researchers and physician-scientists engaged in cancer patient care, the AACR looks forward to continuing to engage with the FDA to ensure that the molecular and genetic diagnostic tests that are being utilized by physicians (and patients) are based on solidly supported scientific evidence."

The president of the American Cancer Society Cancer Action Network, Christopher Hansen, similarly came out in support of proposal. "While early LDTs were relatively simple, low-risk tests, technological advances have created the need for more complete regulation of such tests that provide information that can lead to a specific course of treatment," he said.

"With diagnostic testing and targeted therapies on the rise, the stakes are now higher for cancer patients. LDTs are becoming more numerous, more complex, and have the potential to have a bigger impact on health care decisions.

"Until now, many tests have come to market without independent verification that their results were valid or accurate. This important change will require labs who want to perform lab tests to diagnose diseases where the test is critical to safety, health or a treatment decision to submit information like reports of adverse events to the FDA for review.

"As patients and doctors become more reliant on diagnostic tests to provide this information, it is critical that they are valid and accurate. Cancer patients and survivors commend the FDA for taking this critical step to ensure that patients have access to safe and effective diagnostic tests that can be trusted."

Politics of LDTs

The agency's announcement of its plans for regulating LDTs comes almost a month after five senators urged the Office of Management and Budget to release it.

Sens. Elizabeth Warren (D-Mass.), Edward Markey (D-Mass.), Richard Blumenthal (D-Conn.), Sherrod Brown (D-Ohio), and Dick Durbin (D-Ill.) called on Brian Deese, acting director of the OMB, to release the FDA's draft guidance on the oversight of LDTs, tests that have faced little regulation.

"For years this draft guidance has languished at OMB, causing continued unpredictability and uncertainty for industry, clinicians, patients and the general public," the letter said.

"Once this draft guidance is released it will be open for public comment before being formalized by the FDA, a process that can take an additional significant amount of time. I therefore urge you to take prompt action in releasing this draft guidance on the regulation of laboratory developed tests (LDTs), to ensure appropriate and efficient oversight of diagnostic tools can move forward in an open and transparent manner."

The full text of the letter follows:

Dear Mr. Deese:

I write to urge you to take prompt action in releasing draft guidance on the regulation of laboratory developed tests (LDTs), to ensure appropriate and efficient oversight of diagnostic tools can move forward in an open and transparent manner.

Signed in 1993 by President Clinton, Executive Order 12866 recognized the need for a timely and transparent regulatory review process and set, among other things, a 90-day deadline for the Office of Management and Budget (OMB) Office of Information and Regulatory Affairs (OIRA) to conduct reviews of regulatory policies.

President Obama affirmed his commitment to these standards in Executive Order 13563, stating that the regulatory system must promote predictability and reduce uncertainty. However, key standards have languished at

OIRA, in some cases for several years. One such item is the Food and Drug Administration's (FDA) draft guidance on the regulation of laboratory developed tests (LDTs), some of which could help diagnose specific forms of cancer and other disease conditions.

According to the FDA, laboratories initially manufactured LDTs that were relatively simple, well-understood pathology tests that could be used for low-risk diagnostics or for rare diseases for which adequate validation would not be feasible.

These tests were traditionally developed to be used for a small population of local patients being evaluated by physicians at the same facility where the laboratory was located.

However, over the last decade, increased understanding of genetics and the role particular genes play in disease has led to the creation of new, more complex, medical diagnostic technology. Many of these new diagnostic tools, widely developed and marketed as LDTs, are intended to help diagnose disease earlier, more effectively, less invasively or in many cases, are the only pathology test available to diagnose a medical condition.

These tests and their results are increasingly relied on by patients and medical professionals to help predict the most appropriate course of treatment and care. These tests hold great promise to customize healthcare to be more efficient and targeted for an individual patient.

Because these more advanced LDTs are a staple of clinical decision-making and are being used to diagnose high-risk but relatively common diseases, it is imperative that they perform as they are expected. Incorrect results mean that patients either will not seek out the care and therapy that is needed, or will be subject to treatments that do not work or are harmful.

Recently, the Centers for Disease Control and Prevention (CDC) reviewed a frequently utilized LDT to detect Lyme disease and found "serious concerns" about false-positive results and misdiagnosis. The CDC recommended that the diagnosis of Lyme disease should instead be left to tests approved by the FDA.

Currently, a diagnostic test produced by a manufacturer must first undergo an FDA pre-market review and approval to ensure the test is reasonably safe and effective.

As a part of this review the FDA also assesses the clinical validity of a diagnostic test, which is the accuracy of the test in identifying, measuring or predicting the presence or absence of a clinical condition in a patient.

However, an independent laboratory can develop and use a LDT diagnostic test, for an infinite number of patients, without ever being subject to these same pre-market reviews. This regulatory inconsistency can be confusing and is not always fully understood by either the patient or medical professional relying on LDTs for clinical decision-making.

Despite the fact that FDA has authority to regulate LDTs, under the Food, Drug and Cosmetic Act, historically the agency has exercised enforcement discretion- meaning that it generally did not enforce applicable regulatory requirements for these tests.

According to the FDA, this enforcement discretion was used "because they were relatively simple, low-risk tests performed on a few patients being evaluated by physicians at the same facility as the lab." However, with the advent of more sophisticated, complex, and high-risk LDTs coming to market, the FDA has recognized the importance of ensuring that all new and innovative diagnostic tools are safe and effective for use.

The FDA has developed what the agency has referred to as "risk based" draft guidance on how the agency will exercise its authority over LDTs, while recognizing the unique circumstances of the laboratory community. For years this draft guidance has languished at OMB causing continued unpredictability and uncertainty for industry, clinicians, patients and the general public.

Once this draft guidance is released it will be open for public comment before being formalized by the FDA, a process that can take an additional significant amount of time. I therefore urge you to take prompt action in releasing this draft guidance on the regulation of laboratory developed tests (LDTs), to ensure appropriate and efficient oversight of diagnostic tools can move forward in an open and transparent manner.

Will Craft contributed to this story.

Surgeon General Issues Call To Reduce Skin Cancer Rates

By Will Craft

The surgeon general issued a call to action this week, addressing the rising epidemic of skin cancer in the U.S. and around the world.

Skin cancer is the most commonly diagnosed cancer in the U.S., but is also easily preventable. Billions can be saved on treatment if we adopt new standards and strategies, argued acting Surgeon General Boris Lushniak.

The 102-page document outlines the costs of the disease.

"Each year in the United States, nearly 5 million people are treated for all skin cancers combined, with an annual cost estimated at $8.1 billion," the report reads. "Melanoma is responsible for the most deaths of all skin cancers, with nearly 9,000 people dying from it each year. It is also one of the most common types of cancer among U.S. adolescents and young adults. Annually, about $3.3 billion of skin cancer treatment costs are attributable to melanoma."

The call to action outlined five strategic goals that the surgeon general argues will reduce the rate of skin cancer:

• Increase opportunities for sun protection in outdoor settings.

• Provide individuals with the information they need to make informed, healthy choices about UV exposure.

• Promote policies that advance the national goal of preventing skin cancer.

• Reduce harms from indoor tanning.

• Strengthen research, surveillance, monitoring, and evaluation related to skin cancer prevention.

"Achieving these goals will not be a small task," the surgeon general's office wrote in a summary of the call to action. "It will require dedication, ingenuity, skill, and the concerted efforts of many partners in prevention across many different sectors. Many of these partners are already enthusiastically involved, but greater coordination and support are needed to increase the reach of their efforts. The goals and strategies outlined in the Call to Action are the next steps. We must act with urgency to stop the ever-increasing incidence of skin cancers in the United States."

The report is important because it will help guide people toward a better understanding of how to best avoid skin cancer, some experts say.

"We applaud the Surgeon General for recognizing the need for effective action in decreasing the rates of melanoma in this country," said Tim Turnham, executive director of the Melanoma Research Foundation. "Fighting a public health problem like skin cancer, and specifically melanoma, will require a major cultural shift. This report represents the broad spectrum change of thinking around this healthcare issue we will need to save lives."

The call to action is not without controversy. The American Suntanning Association objected to the inclusion of indoor tanning as a cause of harm in the report.

"The Acting Surgeon General is trivializing an important subject by overstating the role of sunbeds in a cancer that is increasing fastest in older men who do not frequent sunbed salons," the association said in a statement. There may even be benefits to indoor tanning, they argue.

"The report notes that UV exposure can stimulate production of vitamin D in the skin, a vitamin that is important for bone health and other health outcomes. In fact, research suggests that vitamin D may also help prevent numerous chronic diseases, including autoimmune conditions, obesity, diabetes, high blood pressure, heart disease, preterm birth, certain types of cancer, and even all-cause mortality."

PCORI Approves $54.8 Million For Clinical Effectiveness Research

By Will Craft and Matthew Ong

The Patient-Centered Outcomes Research Institute approved $54.8 million for 33 clinical effectiveness projects.

The projects, approved by the institute's board of governors July 29, will study ways to improve outcomes for patients with cancer and other diseases, including diabetes, nervous system disorders, cardiovascular diseases, mental health conditions and kidney diseases.

The studies will compare different approaches to delivering care, improving patient access, and patient-centered clinical effectiveness research methods. Several projects will focus on particular populations, including older adults, minorities, children and low-income individuals.

Selected from 325 applications from funding announcements issued in September 2013, the approved studies are based at institutions and organizations across 18 states. All awards were approved after a

business programmatic review by PCORI staff and issuance of a formal award contract, the institute said.

PCORI is refining their funding announcements to focus on priority topics and larger, pragmatic studies, said the institute's executive director, Joe Selby.

Since it began funding research in 2012, PCORI has approved nearly $549 million in support of 313 research projects and initiatives. The institute said it expects to award about $1 billion in research support by the end of next year.

Nina Bickell, professor of medicine and population health science and policy at Mount Sinai School of Medicine, proposed a three-year, $2 million project to study and improve patient care for late-stage cancer.

"Among advanced cancer patients, discussions about prognosis, goals of care, and end-of-life preferences improve patients' quality of life and reduce hospital and ICU admission rates," the project summary states. "Yet, few patients know their chemotherapy treatments will not cure their disease, despite nearly all wishing to receive both positive and negative information."

Bickell's project seeks to improve goals-of-care discussions by training oncologists to better communicate and understand the effects their discussions have on the patients.

"Current efforts to teach oncologists such skills are impractical; they require a lot of time away from the physicians' office practice and do not take into account job pressures," the summary says.

"Primary outcomes include patient-reported conduct of and satisfaction with the [goals-of-care] discussion. Secondary outcomes include oncologist communication skills; feasibility of performing [goals of care] in the outpatient setting; receipt of care in line with preferences; and use of hospice, chemotherapy, or ICU in the last 30 days of life."

Anonymous $100 Million Gift Moves OHSU Within $82 Million Of Reaching $1 Billion Goal

By Will Craft

The Oregon Health & Science University Knight Cancer Institute moved one step closer to meeting a spectacular fundraising goal.

The institution said it received a $100 million gift from an anonymous donor, leaving the institution 17 months to raise the remaining $82 million needed to match the $500 million challenge set by Nike co-founder Phil Knight and his wife, Penny.

In September 2013, the Knights pledged $500 million to OHSU, as long as the university raised the same amount within two years. (The Cancer Letter, Sept. 27, 2013)

So far OHSU has raised $418 million, with nearly a year-and-a-half left in the challenge, according to the campaign's website.

The cancer center would use the combined $1 billion to help identify cancers in earlier stages.

The $100 million represents the largest private donation in the campaign thus far, and is the fourth-largest donation in the university's history, OHSU officials said. In addition to over 5,000 individual donations to the campaign, the state of Oregon has also committed $200 million to institute facilities. The state's contribution counts toward the matching funds.

"This gift is a tremendous vote of confidence in OHSU and the Knight Cancer Institute," said Director Brian Druker in a statement. "It will enable us to work even more quickly on what we believe is the single most important unmet need in cancer care today—identifying cancers that will become deadly while they are still at a highly curable stage.

L. Keith Todd, president of the OHSU Foundation, thanked the donor.

"This generous gift continues the tremendous momentum of this past year, and we hope it will inspire others who care deeply about curing cancer to make their gifts," Todd said. "Thousands of individuals and organizations from throughout the country have participated in the campaign so far, and several organizations are just launching their own efforts to support the challenge."

A New Way of Funding Research

OHSU plans to use the $1 billion to start a cancer research program that would focus on the molecular characteristics of cancer in order to treat diseases

before they becomes lethal.

"The $100 million anonymous gift will be used to support a full range of Knight Cancer Institute initiatives, including hiring 20 to 30 top scientists and their teams to collaborate on improving methods to identify cancer at its earliest and most curable stage," the university said in a statement. "The $1 billion investment will enable these scientists to focus on discovery and moving the most promising new detection methods and treatments from the laboratory to clinical trials as quickly as possible."

Druker said he wants to see a change in the way cancer research is funded.

"We are facing a disturbing paradox in science," Druker wrote in a guest editorial in this publication (The Cancer Letter, June 13). "We have unprecedented potential for advancements spurred by current technologies. But at the same time we are confronting flat to declining funding."

A central problem, Druker wrote, is that grant funders focus too much on innovation, and not impact. Most grant reviewers can't recognize innovation, and worse, a truly innovative project doesn't stand a chance in today's funding climate, he said.

"Whether we like it or not, progress is made by hard work that advances knowledge, with occasional innovations, so if we demand innovation in all we do, we actually impede progress," Druker wrote. "Instead, we should focus on funding grants that will have an impact or advance a field, while creating environments that foster innovation."

By raising $1 billion, Druker hopes to free scientists of the pain of the grant cycle.

"In our current funding and promotions and tenure system, our focus is on grants and publications," he wrote. "We all know that if our experiments fail, we won't get a publication, which means we won't get a grant and then our faculty position will be in jeopardy. As such, we have created an environment where failure is feared and with funding constraints, these fears are heightened."

The Knight Cancer Institute will be different, he said.

"If the Oregon Health & Science University Knight Cancer Institute is successful in meeting the fund-raising challenge…we will have $1 billion to spend on cancer research," Druker wrote. "As we consider how best to utilize a gift of $1 billion for cancer research, we have decided that we want to create an opportunity for team science in academia.

"The idea is to bring 20 to 30 scientists together, provide them with [Howard Hughes Medical Institute]-like funding, and focus the team on a goal. The goal we have set is to improve our ability to accurately detect lethal cancers at the earliest, most curable state, using an understanding of the molecular characteristics of cancers at this stage."

Letter to the Editor

Expanding the Horizons Of Proton Beam Therapy

By Minesh P. Mehta, Katja Langen and William F. Regine

The Cancer Letter recently published information regarding proton therapy facilities in the U.S., highlighting a contention that 85 percent of patients treated with protons have prostate cancer, the logical implication of which would be that this important resource is utilized minimally for other cancers. In this response, we wish to correct this erroneous impression and also wish to highlight the direction that this technology is moving in.

Proton beam therapy, characterized by its significantly lower total body integral dose relative to photon therapy, is a natural and logical extension of the bioethics concept of "primum non nocere," or "first, do no harm" (1). There is no evidence in the literature, nor is there logical reason to believe that excess radiation to normal tissues (irrespective of whether it exceeds some arbitrarily defined threshold or not) is beneficial to any patient. The logical, almost "tongue-in-cheek" extrapolation of this is that the vast majority of patients eligible for radiation therapy should be considering proton therapy because in almost all instances they will receive a lower radiation dose to their normal tissues; in reality, significantly less than 10 percent of all cancer patients undergoing radiotherapy are treated with proton therapy (2).

There are four critical reasons why proton therapy is not in widespread use at present:

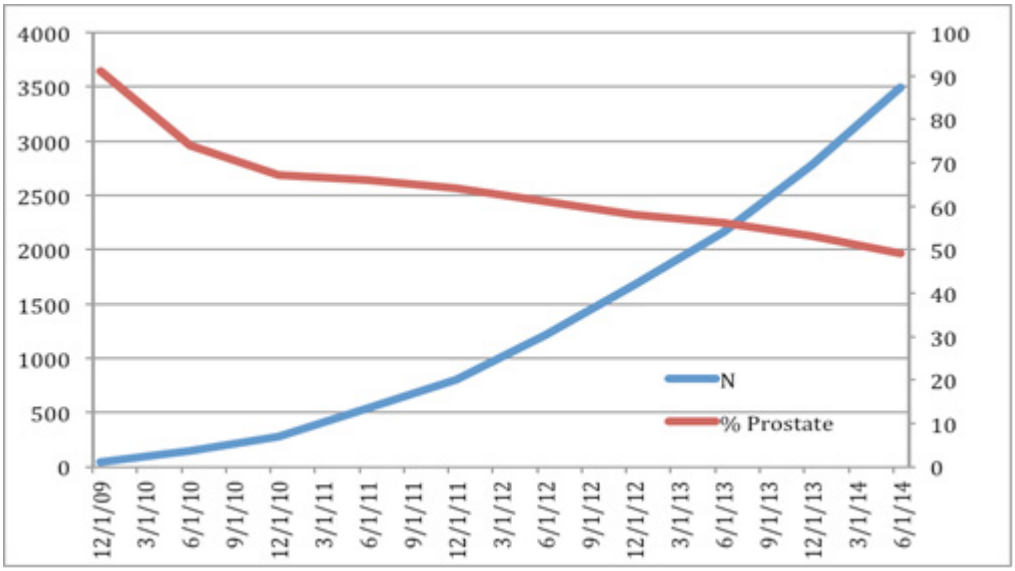
1. Availability: access to proton therapy centers is quite limited; currently, there are only 14 operational centers in the U.S., in comparison to over 2200 conventional photon therapy centers (3).

2. Cost: A key reason for the limited availability of proton therapy is the higher initial construction and subsequent operational costs. Several recent developments are likely to alter this to some extent, explaining the anticipated relatively rapid growth of proton centers in the U.S. in the next decade (4).

3. Measurable clinical benefits: Since a significant proportion of cancer patients have relatively short life expectancy, the long-term benefits of reduced integral

dose to normal tissue may not be realized by some or many of these patients. Further, the relative paucity of completed and published randomized clinical trials demonstrating benefit in terms of reduction in acute toxicity, long-term morbidity, improved tumor control, superior survivorship parameters, etc. has hampered more rapid and broad acceptance of this modality (5).

4. Limited applicability: One often comes across statements such as "Yet about 85 percent of patients who receive proton therapy have prostate cancer", suggesting that the modality has limited applicability and focus (The Cancer Letter, June 20).



Cumulative enrollment on PCG Registry Study for Proton Therapy Outcomes (NCT01255748) between 2009-2014. The dual Y-axis represents total number of patients enrolled with all diagnosis on the left, and percent of these represented by prostate cancer on the right. The percent of patients with prostate cancer is expressed as a cumulative figure, and this has dropped from over 90 percent at initiation to under 50 percent currently, reflecting maturity of the usage of proton therapy and rapidly broadening application to other disease sites.

The landscape in the U.S., and increasingly at a global level, in terms of all four of these issues is likely to change rapidly in the next five to 10 years. First, an evaluation of institutional and industry analysis suggests that at least 24 centers are operational or under construction, interested in, or already pursuing proton therapy, and this will potentially increase and improve access to this modality. A market research firm, ASD Reports, in its latest research report, "US Proton Therapy Market Analysis to 2017," provides a thorough opportunity assessment and clearly states that although proton therapy is in its infancy, there is unprecedented demand for it. They estimate that by 2017, the number of sites providing proton therapy in the U.S. is expected to cross 22.

In part, this growth in proton therapy centers is being fueled by reduced initial capital costs as single or 2-3 room solutions, with more compact architecture, became feasible. In 2013, the first single room facility in the U.S. became operational and several medium sized hospitals are considering this as an option. It is in fact anticipated that future developments in technology will likely further reduce capital costs. In addition, a number of studies which have taken the approach of calculating lifetime costs after a therapeutic intervention, and thereby incorporating the costs of follow-up and management of toxicities, demonstrate that in several situations, although the cost of delivering proton treatment might be higher, lifetime costs are actually lower with this modality, compared to photon therapy (6).

The provision of high-level evidence regarding the value of proton therapy requires the conduct and completion of large-scale multi-institutional clinical trials and to date this effort has been hampered by the very limited number of institutions capable of delivering proton therapy. This scenario is however rapidly changing. The Particle Therapy Co-operative Group (PTCOG) lists in excess of 50 ongoing clinical trials with proton therapy, encompassing an array of malignancies ranging from cancers of the breast, prostate, lung, esophagus, head and neck, base of skull, pediatric, liver, sarcomas, etc. As a larger number of centers participate in these trials, extensive data will be generated, contributing to an explosion in knowledge and evidence in this field. Registry databases, both adult & pediatric, have already started collecting and collating data about patients receiving proton therapy. Accrual to one such multi-institutional registry and

prospective clinical trial database, completely funded at present by member institutions, is approaching nearly 4000 patients. Further, randomized photon verses proton trials previously considered "impossible" or "unethical" are now actually underway (or planned) in several diseases such as prostate cancer, lung cancer, breast cancer, head and neck cancer, glioblastoma, low grade glioma, etc. (7). In fact, by the end of 2014, with support from the NCI, NRG-Oncology will have launched two such major randomized trials, one for lung cancer and the other for brain tumors.

In large measure, this explosive growth in indications and substantial expansion of scope is made possible by a major technological breakthrough in the proton delivery technology, referred to as pencil beam scanning (PBS), which results in further reduction in integral dose (8). Unlike conventional proton therapy, PBS technology allows more complicated and larger targets to be treated. Not surprisingly, therefore, the focus of modern pencil beam scanning proton therapy is on a wide range of malignancies.

Although precise numbers regarding the utilization of particle beam therapy in the US for various cancer indications are not readily available, a review of the data from tumor registries allows some insight. The Proton Collaborative Group (PCG), a multi-institutional collaborative effort by multiple proton centers has maintained a comprehensive prospective registry trial since 2009. Figure 1 below demonstrates that through June 2014, 3497 patients were entered on this online Registry Study for Proton Therapy Outcomes (NCT01255748). The cumulative percentage of prostate cancer patients has dropped dramatically from more than 90 percent initially, to 74 percent within six months, and has consistently declined at each semi-annual evaluation to under 50% at present; this is a far cry from the wildly speculative 85 percent contention, In fact, because this is a cumulative percentage, prostate cancer currently accounts for significantly lower actual proportions (personal communication, Megan Dunn, PCG Coordinator 7/14/14).

The introduction of the newer PBS systems has opened up the indications that were difficult to treat with conventional proton therapy. For example, the treatment of complex head and neck targets is now possible at centers that have access to PBS and they represent a significant patient fraction at these centers. At the University of Texas MD Anderson Cancer Center, one of the busiest U.S. proton facilities, over a seven-year timeframe from 2006-2013, 4,521 new patients were treated with proton therapy, of whom 43 percent had prostate cancer. An evaluation of time trends shows a significant drop in the proportion of patients with prostate cancer from 2006 through 2013, especially after the introduction of PBS, with commensurate increase in the proportion of more complex cases; for example, the proportion of all proton treated cases accounted for by genitourinary tumors dropped from 35 to 32 to 25 percent from 2012-2014. (NAPT Conference, Washington DC, 2014, Steven J Frank, MD, Proton Center Medical Director). The National Proton Therapy Consortium, a member organization, is currently surveying its U.S. membership and in the near future shall be able to provide insights regarding these numbers from an even larger cohort of centers. Most current centers have added or will add PBS technology while some of the newer facilities will use PBS exclusively. The patient mix will likely broaden accordingly.

Therefore, it is very safe to headline "Proton Therapy: Not Just for Prostate Cancer" as today's reality, rather that perpetuate an inaccurate myth regarding its utilization, and more importantly, an inaccurate reflection of its potential.

So where is proton therapy headed? The recent recognition that there is no safe dose to the heart for women with breast cancer receiving radiotherapy will likely lead to large scale evaluation of the role of proton therapy to minimize cardiac dose (9). A large multi-center randomized trial to evaluate this is already in the planning stages. Malignancies where significant reduction in dose to mucosal tissues can be achieved, e.g. head and neck cancer, might be logical to consider for randomized evaluation of reduction in acute toxicity and improvement in patient-centered outcomes. A number of these trials are also already underway or in the planning stages. In diseases where dose-escalation and normal tissue sparing is a required strategy, such as lung cancer and brain tumors, randomized trials are also already underway. Hypofractionation remains a major area of exploration and in particular, if combined with surgery in a pre-operative fashion, might lead to a number of paradigm-changing approaches. The sparing of large volumes of bone marrow, especially in combined chemo-radiotherapy approaches, such as is the case with pelvic neoplasm, craniospinal irradiation, etc., remains a major testable hypothesis for proton therapy. Newer PBS centers are also being equipped with on-board volumetric imaging that will significantly enhance the process of patient set-up verification, and improve tumor visualization at the

time of treatment. The improved precision made possible by "image guided" proton therapy (IGPT) will enhance the treatment capabilities of PBS, especially for tumors that are currently challenging, such as lung cancer and tumors in the upper abdominal region (e.g. within the liver/pancreas). So acknowledging the well-known automobile commercial, it is fair and appropriate to headline that "today's proton therapy is not your father's proton therapy, and is not just for prostate cancer." The horizons of proton beam therapy are indeed expanding rapidly.

Mehta is a professor of radiation oncology at the University of Maryland School of Medicine, and is medical director of the Maryland Proton Treatment Center.

Langen is an associate professor of radiation oncology at the university and is associate chief of proton physics at the treatment center.

Regine is the Isadore and Fannie Schneider Foxman Chair and Professor of Radiation Oncology at the university and serves as executive director of the treatment center.

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In Brief

IOM Cancer Policy Forum Names Six At-Large Members

(Continued from page 1)

The IOM established the National Cancer Policy Forum to serve as a venue for national leaders from multiple sectors to work cooperatively to address high-priority cancer policy issues.

The new at-large members are:

• **Lucile Adams-Campbell**, professor of oncology, associate director for minority health disparities research, Georgetown University Medical Center Lombardi Cancer Center.

• **Kenneth Anderson**, Kraft Family Professor of Medicine, American Cancer Society Clinical Research Professor at Harvard Medical School, and director of the Jerome Lipper Multiple Myeloma Center at the Dana Farber Cancer Institute.

• **Lori Hoffman Hōgg**, cancer program director of the Albany Stratton VA Medical Center.

• **Samir Khleif**, director of the Georgia Regents University Cancer Center .

• **Jennifer Pietenpol**, director of Vanderbilt-Ingram Cancer Center, and Benjamin F. Byrd, Jr. Professor of Oncology and professor of biochemistry at Vanderbilt University Medical Center.

• **Deborah Schrag**, professor in the Department of Medicine of Harvard Medical School, and chief of population sciences at the Dana-Farber Cancer Institute.

At-large members who rotated off the forum include Fred Appelbaum, Peter Bach, Edward Benz, Micheale Christian, Bob Erwin, Roy Herbst, John Mendelsohn, and John Wagner.

Panel participants include clinicians, patients, researchers, professional and advocacy organizations, pharmaceutical manufacturers and policymakers. During the most recent meeting, members examined the issue of escalating treatment costs, as well as shortages of some cancer drugs and the impact of these issues on cancer patients and their families.

ALLYSON KINZEL was named vice president for institutional compliance and chief compliance officer at MD Anderson Cancer Center.

Kinzel most recently served as associate vice president and deputy chief compliance officer. She will oversee compliance attorneys and staff.

She succeeds Jessica Quinn, who was named to a senior vice president position with Ohio Health. Before joining MD Anderson, Kinzel represented health care providers as a partner at Baker Hostetler, LLP, and as an attorney at Vinson and Elkins, LLP. She is also past-president of the Houston Bar Association's Health Law Section.

MICHAEL SAPIENZA received the 2014 David Jagelman, MD, Award for Advocacy in Colorectal Cancer from **the American Society of Colon and Rectal Surgeons**.

Sapienza, founder and executive director of the Chris4Life organization, accepted the award during the society's annual meeting in Hollywood, Fla. Chris4Life is a national colon cancer nonprofit founded by Sapienza after losing his mother to colon cancer in 2009.

The award honors the memory of David Jagelman, who founded and directed the Cleveland Clinic's Familial Polyposis Registry and became chairman of the Department of Colorectal Surgery at the Cleveland Clinic Florida when he died from kidney cancer in 1993, at age 53.

JOEL HELMKE joined **WellStar Health System** as corporate vice president of oncology services.

Helmke served as division administrator of internal medicine and managed four clinical centers and nine academic departments at MD Anderson Cancer Center, where he held leadership positions for 14 years.

Helmke will assist WellStar in the further development of the oncology program, and will have operational leadership of the cancer registry, radiation oncology, infusion, navigators and CyberKnife.

W. MICHAEL ALBERTS received the honorary title of master fellow from the **American College of Chest Physicians**. Alberts is chief medical officer of Moffitt Cancer Center.

The designation is the highest level of recognition awarded by the organization and is given for achievement of professional prominence in chest medicine. Alberts will be the 33rd recipient, when he is conferred during a convocation ceremony in October.

NCI announced the consolidation of NCI central communications functions into the new **Office of Communications and Public Liaison**. The office will bring together the Office of Communications and Education, the Office of Media Relations, and the Executive Secretariat.

Peter Garrett will head the office, after joining NCI last December as special advisor for communications. Nelvis Castro will serve as OCPL's deputy director. Castro

has served as acting director since the departure of Lenora Johnson, the previous director of communications.

Diagnosing breast cancer costs more in the U.S. than in Europe, according to a study produced by iData, a market research firm.

European health authorities spend just under 60 percent the amount spent in the U.S., even though they purchased 500,000 more biopsy needles last year, according to researchers. Europe sees more than four times the purchases of inexpensive, spring-loaded core needles, said Kamran Zamanian, president and CEO of iData. The U.S. market focuses on more expensive minimally invasive technologies.

According to the study, Hologic Inc. leads the U.S. breast cancer needle market in vacuum-assisted breast biopsy devices.

The report estimates that the European market for breast cancer needles will grow by $10 million over the next five years, whereas the U.S. market is expected to grow by $33 million.

FDA News

FDA Approves Zydelig Tablets In Three B-Cell Blood Cancers

FDA approved Zydelig (idelalisib) tablets for the treatment of three B-cell blood cancers.

Zydelig is indicated for patients with relapsed chronic lymphocytic leukemia in combination with rituximab for whom rituximab alone would be considered appropriate therapy; as monotherapy for patients with relapsed follicular B-cell non-Hodgkin lymphoma; and for small lymphocytic lymphoma patients who have received at least two prior systemic therapies.

Accelerated approval was granted for the follicular B-cell and small lymphocytic lymphoma indications based on overall response rate. Zydelig is a first-in-class inhibitor of PI3K delta, a protein that is over-expressed in many B-cell malignancies and plays a role in the viability, proliferation and migration of these cancer cells.

Approval in CLL is supported primarily by data from a randomized, placebo-controlled phase III trial of Zydelig plus rituximab in 220 patients with relapsed CLL who were not able to tolerate standard chemotherapy.

The study was stopped early in October 2013 by an independent data monitoring committee due to a highly statistically significant benefit in progression-free survival in the Zydelig arm as compared to those receiving rituximab alone [HR=0.18 (95% CI: 0.10, 0.32), p<0.0001].

Median PFS was not reached in the Zydelig plus rituximab arm (95% CI: 10.7 months, NR) and was 5.5 months in the placebo plus rituximab arm (95% CI: 3.8, 7.1). FDA granted Zydelig a Breakthrough Therapy designation for relapsed CLL.

Zydelig's accelerated approval in FL and SLL is supported by data from a single-arm phase II study of Zydelig monotherapy in patients refractory to rituximab and alkylating-agent-containing chemotherapy (FL: n=72; SLL: n=26).

In the study, Zydelig achieved an overall response rate of 54 percent and 58 percent, respectively, in FL and SLL patients. Of the responses seen in FL patients, 8 percent (n=6) were complete responses; all 15 responses in SLL patients were partial responses. The median duration of response was 11.9 months in SLL patients (range: 0.0, 14.7 months) and median duration of response was not reached in FL patients (range: 0.0, 14.8 months). Improvement in patient survival or disease related symptoms has not been established in these indications.

FDA has also approved a risk evaluation and mitigation strategy for Zydelig. The purpose of the Zydelig REMS is to inform healthcare providers of the serious risks of hepatotoxicity, severe diarrhea, colitis, pneumonitis and intestinal perforation. Zydelig is marketed by Gilead Sciences.

FDA approved Imbruvica (ibrutinib) capsules for the treatment of patients with chronic lymphocytic leukemia who have received at least one prior therapy. Imbruvica was also approved for CLL patients with del 17p.

The update to the Imbruvica label is based on data from the phase III RESONATE study, which demonstrated Imbruvica significantly improved progression-free survival and overall survival compared to ofatumumab in patients with previously treated CLL or small lymphocytic leukemia.

Imbruvica is jointly developed and commercialized by Janssen Biotech Inc. and Pharmacyclics Inc.

Imbruvica was initially approved in February 2014 through the FDA's accelerated approval process, based on data from a phase Ib/2 study for patients with CLL who have received at least one prior therapy. This indication was based on an overall response rate.

In accord with the accelerated approval process, confirmation of clinical benefit in a subsequent phase III trial was required, which has resulted in this updated

indication for the use of Imbruvica in patients with CLL who have received at least one prior therapy and in CLL patients with del 17p.

The randomized, international, open-label RESONATE trial enrolled 391 patients with CLL or SLL who had received at least one prior therapy; 32 percent of whom had del 17p.

Patients were administered either 420 mg oral ibrutinib (n=195) once-daily until progression or unacceptable toxicity or intravenous ofatumumab for up to 24 weeks (n=196, initial dose of 300 mg followed by 11 doses at 2,000 mg per dose and schedule consistent with local labeling).

Data showed single-agent, once-daily Imbruvica significantly prolonged PFS (median not reached vs. 8.1 months; HR 0.22, 95% CI, 0.15 to 0.32; P<0.0001) and OS (HR 0.43; 95% CI, 0.24 to 0.79; P=0.05) versus intravenous ofatumumab in previously treated patients with CLL or SLL. The OS results represent a 57 percent statistically significant reduction in the risk of death in patients receiving Imbruvica versus those in the ofatumumab arm.

PFS was the primary endpoint of the RESONATE study, with OS, ORR and safety as key secondary endpoints. Imbruvica was associated with a 78 percent statistically significant reduction in the risk of death or progression versus ofatumumab. ORR was shown to be 42.6 percent in the Imbruvica arm, versus 4.1 percent in the ofatumumab arm.

Data from this study were recently presented during an oral session at the annual meeting of the American Society of Clinical Oncology and simultaneously published online in the New England Journal of Medicine.

FDA granted Priority Review for Avastin plus chemotherapy for the treatment of persistent, recurrent, or metastatic cervical cancer.

The drug's sponsor, Genentech, submitted a supplemental biologics license application based on data from the phase III GOG-0240 trial. The application has an FDA action date of Oct. 24. Genentech is a member of the Roche Group.

GOG-0240 is an independent, NCI-sponsored study that assessed the efficacy and safety profile of Avastin (bevacizumab) plus chemotherapy (paclitaxel and cisplatin or paclitaxel and topotecan) in women with persistent, recurrent or metastatic cervical cancer.

Data from 452 women showed that the study met its primary endpoint of improving overall survival with a statistically significant 29 percent reduction in the risk of death for women who received Avastin plus chemotherapy compared to those who received chemotherapy alone (median OS: 17.0 vs. 13.3 months; HR=0.71, p=0.004).

Women in the Avastin plus chemotherapy arm also lived longer without disease worsening compared to those who received chemotherapy alone (median PFS: 8.2 vs. 5.9 months; HR=0.67, p=0.002). There was no increase in treatment-related deaths in the Avastin plus chemotherapy arm as compared to the chemotherapy alone arm.

Imbruvica received a positive opinion by the Committee for Medicinal Products for Human Use of the European Medicines Agency and was recommended full marketing approval for the treatment of two blood cancers.

The CHMP recommendation for Imbruvica (ibrutinib) is for the treatment of adult patients with relapsed or refractory mantle cell lymphoma, or adult patients with chronic lymphocytic leukemia who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemotherapy or immunotherapy.

The positive opinion was based on data from a phase II study (PCYC-1104) in MCL, and a phase III study (RESONATE; PCYC-1112-CA) and a phase II study (PCYC-1102) in CLL.

Imbruvica is being jointly developed and commercialized in the U.S. by Pharmacyclics and Janssen Biotech Inc. In Europe, once approved, Janssen-Cilag International NV will be the marketing authorization holder. Imbruvica received accelerated approval from FDA for the treatment of patients with MCL and CLL who have received at least one prior therapy.

FDA issued a drug safety communication warning that the intravenous chemotherapy drug docetaxel contains ethanol, which may cause patients to experience intoxication or feel drunk during and after treatment. FDA is revising the labels of all docetaxel drug products to warn about this risk.

Docetaxel is a prescription chemotherapy drug used to treat different kinds of cancer, including cancers of the breast, prostate, stomach, head and neck cancers, and non-small-cell lung cancer.

FDA says healthcare professionals should consider the alcohol content of docetaxel when prescribing or administering the drug to patients, particularly in those whom alcohol intake should be avoided or minimized and when using it in conjunction with other medications.