



FIT COLONOSCOPY STOOL DNA TEST

FDA Advisory Panel Unanimously Favors New Stool DNA Colorectal Screening Test

By Matthew Bin Han Ong

The FDA Molecular and Clinical Genetics Panel voted 10-0 to recommend approval of Cologuard—a noninvasive, multitarget stool DNA screening test for colorectal cancer.

Sponsored by Exact Sciences Corp., Cologuard outperformed a standard fecal immunochemical test [in a study published March 19](#) in the New England Journal of Medicine.

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Federal Funding

Rising Costs at NCI Threaten to Overtake Slim Increases In Budget Appropriations

By Conor Hale

Sometimes a funding increase can be no increase at all.

NCI's budget was increased by 2.8 percent for the current 2014 fiscal year, or about \$134 million, restoring about 53 percent of previous cuts made by sequestration. The institute's total budget stands at \$4.9 billion.

However, this increase did not translate into an extra 2.8 percent for all of NCI's programs. Mandatory costs also grew at the same time—salaries and benefits, building utilities and rent, and telecommunications infrastructure and security—all increased by about \$45 million in total, leaving only \$89 million to be spread around NCI's research programs.

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In Brief

Caplan Receives NSB Public Service Award

ARTHUR CAPLAN received the 2014 Public Service Award from the **National Science Board**. Caplan is the founding head of the Division of Bioethics at New York University Langone Medical Center.

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Imperiale: Cologuard Sensitivity As High as Colonoscopy

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The advisory panel, part of the Medical Devices Advisory Committee, recommended March 27 that Cologuard be approved for use in conjunction with colonoscopy and other test methods, in accordance with recognized screening guidelines.

Cologuard was tested against FIT in a cross-sectional study at 90 sites in the U.S. and Canada in persons at average risk for colorectal cancer. The study, DeeP-C, enrolled 12,776 participants, and 9,989 had results that could be fully evaluated.

Cologuard detected 92.3 percent of the 65 participants diagnosed with colorectal cancer on colonoscopy. FIT detected 73.8 percent ($p=0.002$) of the colorectal cancers.

The panel's unanimous vote—which is almost certain to lead to approval—is important for the gastroenterology community, because Cologuard's high sensitivity and noninvasive sample collection could make it a viable alternative to colonoscopy, even if it's not labeled as a replacement for colonoscopy.

The price for Cologuard has not been set, but Exact Sciences has indicated that it's likely to cost about \$500 per test. The price of a regular colonoscopy can be as low as below \$1,000 or as high as \$5,000, depending on where the procedure is performed. The choice of anesthesia affects the price, as does the need for biopsies.

"I think there is some chance that some

gastroenterologists may feel threatened by the test," said Thomas Imperiale, principal investigator of the DeeP-C study and lead author of the NEJM paper. "But if it leads to unscreened people getting screened, that is what is most important."

"Screening colonoscopy is not going away. Those who had a good experience with screening colonoscopy will likely be willing to have it again," said Imperiale, professor of medicine in the Division of Gastroenterology and Hepatology at Indiana University School of Medicine. "And for those who have not had a colonoscopy, it will bring more people to screening. That's the hope this test holds."

"Extending options with another non-invasive test that could be done less frequently than every year should appeal to some people who have stayed away from screening."

The test is intended for patients who are typical candidates for colorectal cancer screening: people of 50 years or older.

Sample collection for the stool DNA test requires the user to send an entire bowel movement, no more than 300 grams, to a laboratory. Unlike FIT, which uses a brush to collect a small stool sample, Cologuard's test kit comes with a container held in a bracket for placement in a toilet seat.

Cologuard's sensitivity for detecting advanced precancerous lesions was 42.4 percent with DNA testing and 23.8 percent with FIT ($p<0.001$).

"Cologuard does not have higher sensitivity than colonoscopy," Imperiale said. "It may be as high for cancer, but it depends on how you define cancer sensitivity for colonoscopy."

Cologuard is an important adjunct to colonoscopy by offering a noninvasive means of screening for colorectal cancer, said Andrew Chan, a member of the American Gastroenterological Association Research Policy Committee, as well as an associate professor of medicine and director of Gastroenterology Training at Massachusetts General Hospital.

"I don't view Cologuard as the replacement for colonoscopy," Chan said to The Cancer Letter. "I think we do need to identify effective noninvasive methods of screening, because we do recognize that there is a portion of the population for whom primary colonoscopy screening is not necessarily an option."

"So it's important to have additional options for patients for whom primary endoscopic screening is not going to be employed. Up to this point, we felt that the noninvasive methods that were available such as fecal occult blood testing that had limitations. I think it is

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important for us to recognize that there are new options that are more effective that can be certainly employed in a way that really complements what we can do with colonoscopy.

“I do think that the field will recognize the importance of having this in our armamentarium,” Chan said. “I think it’s going to be something that people will reach for as an option compared to the currently available noninvasive methods.

“I think, at this point, we don’t yet understand the role of Cologuard or noninvasive testing as follow-up or surveillance. I think that’s an important question that needs to be addressed in the future, in terms of efficacy for surveillance, but also how it would influence cost. So there are definitely studies and data that need to be generated to really assess it relative to repeated colonoscopy over time.

“There are also important studies that need to be done regarding the cost-effectiveness of this kind of test relative to other programs so that we can really get a sense of how it might fit from a societal perspective,” Chan said. “There’s both the clinical effectiveness that needs to be determined, but also the overall impact it may have on public health with respect to costs to the system—those are areas that still need to be addressed.”

The development of stool DNA testing is a “success story,” according to [an NEJM editorial](#) by Douglas Robertson, associate professor of medicine at the Dartmouth Institute and chief of gastroenterology at White River Junction, VT, VA Medical Center, and Jason Dornitz, an outcomes researcher in gastroenterology and professor and national program director for gastroenterology at the Department of Veterans Affairs at the University of Washington.

“The test itself is inherently attractive, since it leverages knowledge of the biologic pathways leading to colorectal cancer,” they wrote. “Early attempts to identify genetic and epigenetic changes in stool were fraught with challenges. In the first large-scale evaluation of stool DNA screening, only half of the 31 invasive cancers and less than 20 percent of advanced adenomas, were detected.

“However, substantial work has been done to improve the technology, including altering the market panel and the collection buffer. Furthermore, a test for human hemoglobin was added to the genetic panel, and an algorithm was developed to determine a positive test from the individual assays.”

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Lower Specificity and a Higher False Positive Rate

The primary performance measures of the study were Cologuard’s colorectal cancer sensitivity and Cologuard advanced-neoplasia specificity. The sponsor excluded advanced adenomas from the specificity calculation, considering these to be positive outcomes since they are treated during colonoscopy.

The primary objective for Cologuard colorectal cancer sensitivity was a 95 percent one-sided lower confidence bound exceeding 65 percent. The primary objective of Cologuard advanced-neoplasia specificity was a 95 percent one-sided lower confidence bound exceeding 85 percent.

The test had a specificity rate of 86.6 percent compared to 94.9 percent for FIT among participants with nonadvanced or negative findings ($p < 0.001$), 89.8 percent and 96.4 percent, respectively among those with negative results on colonoscopy ($p < 0.001$).

“Although high sensitivity is the most important attribute of cancer-screening tests, specificity is also important, since it affects the number of persons who have positive test results, a majority of whom will have false positive results because of the low prevalence of cancer,” the NEJM paper reads.

The specificity of FIT (94.9 to 96.4 percent) was superior to that of the DNA test (86.6 to 89.8 percent), with false positive rates ranging from 3.6 to 5.1 percent and 10.2 to 13.4 percent, respectively.

Positive results on the DNA test increased the probability of identifying colorectal cancer from 0.7 to 3.7 percent, as compared with 6.9 percent for FIT, and increased the probability of identifying an advanced precancerous lesion from 7.3 to 19.9 percent, as compared with 25.9 percent for FIT.

“The lower specificity is something that has to be figured out quantitatively, and that’s the kind of thing the U.S. Preventive Services Task Force will do,” said David Ransohoff, co-author of the NEJM paper and a cancer screening researcher and gastroenterologist at the University of North Carolina. “What happens if you have a false positive is that you get a colonoscopy, as many people would get otherwise.

“The task force is going to have to figure out quantitatively how many, and is this a disadvantage in terms of potential complications, costs and effort, and just what do those numbers look like, and so that has to be figured in.

“It’s different than a false positive for, say, an ovarian cancer test blood test where you might eventually get an operation. The consequence here is just another screening test—a colonoscopy—that you

might have gotten otherwise,” Ransohoff said to *The Cancer Letter*.

“The reality, though, is if you do this test multiple times over 20 years, that’s going to likely add up to a relatively high chance that at some point in those 20 years you are going to end up with a colonoscopy, and that will have to be figured in—what are the costs, whether it’s dollars or just effort in risks or complications.”

Imperiale and Ransohoff have no financial conflicts of interest.

“I know that Exact Sciences is going to have to do a post-approval study to look at the lower specificity, and to determine what the predictive values are and the yields are over time, at least in the short term, perhaps a three-year study,” Imperiale said. “But the so-called high false positive rate, in part, occurred in the study because we classified people who had non-advanced neoplasia—as not having disease.

“Clinically, they are not treated as not having disease. When those patients get colonoscopy and they have those same non-advanced adenomas found, they get put into surveillance protocols. So, in a sense, colonoscopy lacks specificity to as great, or perhaps a greater extent than this test, but the fact is that the specificity of colonoscopy is not 90 percent. There is just no way. It depends on what your outcome is.

“So if you eliminate that group that’s got clinically ignorable disease, namely, non-advanced adenomas, then you are dealing with about a 10 percent false positive rate, and there’s probably going to be variation in that rate by age, such that people who truly have no lesions on colonoscopy who are in the younger age range, may have a specificity that’s as high as 93 or 94 percent.

“So, this is a big study—10,000 people—but at the end of the day, the numbers are such that the number of advanced adenomas and cancers really doesn’t allow this degree of subgroup analysis and we are going to just have more data over time as the test is used to find where it fits in, how well it belongs, where it belongs in the scheme of colon cancer screening.”

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The Panel's Comments

“I typically refrain from commentary, but I will say this: I think this is a phenomenal study, in particular, for one reason,” said FDA panel member Ronald Przygodzki, acting director of Biomedical Laboratory Research and Development at the Department of Veterans Affairs Office of Research & Development.

“You are actually identifying people with the large sessile adenomas. You are looking at the large polyps you would not otherwise find, and now, you have the greater potential to actually cure those individuals.”

FDA approval usually follows the advisory committee recommendations, but chances of approval rise sharply when the committee’s vote is unanimous.

“I’d like to also say this is a great study, really well-designed, a team that spans the spectrum of all the disciplines needed to execute this,” said panel member Steven Skates, associate professor in the Department of Medicine at Harvard Medical School and associate in biostatistics (medicine) at the Massachusetts General Hospital Cancer Center. “I like the fact that you locked software down before the study was started. I think that’s very important. It’s a great deal of reassurance that there wasn’t any tweaking going on after the results came in so that you change the cutoffs, optimize things.

“I think, just having a sense of the past 20 years being in early detection, this is one of the biggest improvements in early detection that I’ve seen, and so, congratulations to everyone involved, particularly the statisticians—they often get left out.”

The data in this study are solid, concurred David Gates, the panel’s industry representative, and senior director and for regulatory affairs at Roche Molecular Systems, Inc.

“That’s always kind of a thing of beauty,” Gates said. “I think they did a very good job on showing, also, the fact that it picks advanced adenomas that are higher rate—it’s a good thing in terms of being able to pick up precursors sooner and I think it’s a good test.”

Next Step: The USPSTF

The stool DNA test will likely be considered by the U.S. Preventive Services Task Force in its review of colorectal screening guidelines.

“I think the world is going to seriously have to consider further the role of indirect tests in programs of colon cancer screening and that the important assessment will be that of the U.S. Preventive Services Task Force, which will do modeling about what the clinical impact and tradeoffs, pros and cons, may be of this, and other strategies,” Ransohoff said to *The Cancer*

Letter. “And part of the challenge for the task force is that this study has no data about test interval—what happens in a program of screening over time.

“First, colonoscopy is a really important test, and when a primary non-invasive screening test is positive, colonoscopy is what you do, and that’s what the intervention is,” Ransohoff said. “The question on the table is whether colonoscopy should be the preferred primary screening test, which the task force does not say it should be. However, other guidelines organizations dominated by gastroenterologists suggest that it should be, and that’s a big tension, that’s a big issue.”

AGA’s Chan said it’s “premature” for USPSTF to make a recommendation of Cologuard “in the absence of the kind of studies that need to be done.”

“I think we still don’t have the data to show that Cologuard can be used as a replacement for modalities for surveillance—that’s still something that will need to be studied,” Chan said.

USPSTF is regarded as the most neutral guideline-making organization, and, under the Affordable Care Act, high grades from the task force determine whether insurers would cover the tests (The Cancer Letter, [March, 21](#)).

“The task force has historically been the gold standard for guidelines-making organizations, because of its very explicit, deliberate and quantitative process, and because its recommendations are generally neutral,” Ransohoff said. “In contrast, other guidelines may have a less-clear and less-elaborate process and may have conflicts of interests among the people making guidelines.

“And what we are seeing here is an even better primary screening test, than those that, in the past, the USPSTF has been satisfied with. The task force has been satisfied in the past—based on its analysis of evidence and modeling—with indirect tests that are less good and less sensitive than this test. The task force has been happy in the past with guaiac-based FOBT test, which is much less sensitive. They don’t prefer one over the other—they say any of several strategies is adequate.

“The task force is now charged with considering not only benefit and harm to patients, which has been their main concern since they were created, but also with cost and factoring in cost. And its high-level recommendations—A and B—are going to be reimbursed by government. In other words, cost is now going to have to be factored in by them. Cost is important, but the question is, who should do it. Should it be the task force, or political organizations like Congress?

“Many people in the medical profession feel that the task force should focus mainly on evidence and benefit and harm, rather than making value judgments about amounts of money spent and so forth. That’s going to get made, but it shouldn’t be the task force. There’s an issue on how the money and business is going to get handled.

“The task force is going to look at this—they have already stated that they are in the process of re-reviewing things and they will look at the evidence and do their modeling, and will very likely make some determination on their own, but this may be going on the order of a year,” Ransohoff said.

“Cost is going to end up being a practical real world limitation that the doctors and patients and the payors are going to have to figure out, and the collection method may well be acceptable to many people but some people may not like it. All those things will just have to be worked out in the real world.”

The role of Cologuard in colorectal screening should come to the task force, Imperiale said.

“The FDA approval is certainly not the only thing that test needs to go forward, obviously,” Imperiale said. “It needs approval from guidelines organizations and the U.S. Preventive Services Task Force—that would be the single most important group to get approval.

“I think to the extent that they rely on modeling, they may want to see what the projected outcomes are from using this test at different intervals over time, and I’m not sure about whether Medicare or CMS would want that data before deciding on whether they would cover it and how much they would pay for it.

If the 35 percent of people who are unscreened went for Cologuard right now, gastroenterologists would be overwhelmed, Imperiale said.

“We would not be able to keep up with the volume,” Imperiale said. “And if people who have colonoscopy opted for this test instead, it would decrease some of the positive patients, because not as many of patients would get colonoscopy.

“If we would not identify those non-advanced adenomas, we would be doing less surveillance—that is arguably a good thing, so it’s possible that we could even increase efficiency of it by using the test,” Imperiale said.

“So I think it all depends on approval, recommendation and then of course, ultimately, the deciders will be the patients themselves.”

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Ransohoff: Cologuard To Define the Roles of Colorectal Tests

Addressing the Molecular and Genetics Screening Panel, David Ransohoff, coauthor of the NEJM paper, focused on the future role of noninvasive tests like Cologuard in programs of screening for colorectal cancer.

The text of Ransohoff's remarks during the public hearing segment of the March 27 meeting follows:

I will discuss noninvasive tests in colon cancer screening, and address, first, if colonoscopy is the best test, second, the need to consider programs of screening using noninvasive tests, because programs of noninvasive testing, over time, may be better than a program of colonoscopy.

My career has focused on screening, including the process to evaluate diagnostic tests, evaluation of cancer screening tests including those listed here, screening policy and the process to make guidelines more trustworthy.

My conflicts and relationships include sponsors. To Exact as a paid consultant until 2002. Since 2002, no financial interests. For Epigenomics, no financial interests. For FDA, I am a member of a devices panel.

Today, I speak for neither sponsor. My reason to speak is to address FDA's concerns regarding guidelines and recommendations about noninvasive tests.

FDA said in the Federal Register that it wants a test to be used in accordance with recognized screening guidelines but then noted in its executive summary that recommendations differ—some say colonoscopy is preferred.

So, is colonoscopy the preferred gold standard best, and what is the role of indirect tests?

My comments are concerned with how guidelines differ, why, and which to trust, and what the role of indirect tests is, and how we assess that.

The major screening guidelines differ, as FDA noted, in what they say. The American Cancer Society/Multi-Society Task Force (multiple GI societies) and the American College of Radiology endorsed indirect methods like fecal occult blood testing, but also state a structural exam is preferred—which was interpreted as colonoscopy is preferred.

In contrast, U.S. Preventive Services Task Force concludes that any of several programs including occult blood testing is acceptable.

This phrase, "structural exam preferred," received intense attention of doctors in gastroenterology and primary

care, and was interpreted as colonoscopy is preferred.

Why the difference?

The answer is process—the process to make guidelines differed.

In the 2008 ACS/Multi-Society Task Force, there were no pre-stated rules of evidence, no assessment of outcomes of benefits and harm quantitatively, and conflict of interest was not managed. The process, involving mainly gastroenterologists and radiologists, not generalists and methodologists, was described as political, in print, by a panelist.

The U.S. Preventive Services Task Force handles this process better—that is why the "yeses" [in the table in the slide] are there. The USPSTF, in assessing evidence, uses a quantitative analytic framework resembling a clinical trial. I know you can't read this, but the test is done here, the indirect tests are done here, outcomes are measured here, and there are lots of steps that happen in between, as if you were doing a trial.

These differences in process between the two sets of guidelines were noted in the Institute of Medicine's Clinical Practice Guidelines We Can Trust report in 2011, in a case study in the box over here, comparing the two guidelines. There were deficiencies in the ACS Multi-Society Task Force guideline that had said colonoscopy preferred; that guideline was less trustworthy.

Indeed, these events prompted the American Cancer Society to devise and describe, in this article in JAMA (2011), an entirely new guidelines-making process evolved from the old.

The events illustrate, then, in the field of guidelines, that FDA and others will consider, that not all guidelines are created equal. That's one thing that this example illustrates.

Last, and that's also illustrated by this example, how can colonoscopy not be best? The USPSTF's quantitative analysis shows how.

At any one application, colonoscopy is best because it's very sensitive and can detect lesions and remove them. But in a program of screening colonoscopy every 10 years, for example, it may miss new or rapidly growing lesions that may be detected by less-sensitive, noninvasive tests done more frequently.

And this means that we need to consider program sensitivity and specificity as well as application sensitivity and specificity. And program sensitivity and specificity depends, as we heard Dr. Tzou (Abraham Tzou, from FDA) start to describe this morning on issues like test independence, which are related to biology,

growth rates over time, whether over time lesions get mutations and so forth. Questions not addressed in one-point-of-time studies.

In conclusion then, guidelines do differ. The colonoscopy-best guidelines are not as trustworthy as the USPSTF's.

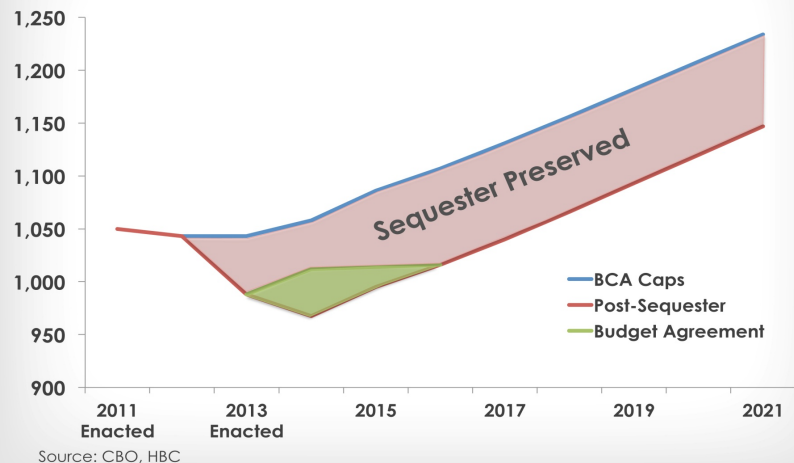
For the USPSTF, programs of some noninvasive tests have, historically, been supported by the task force.

As these kinds of tests may improve, such tests may continue to have an important role. The bottom line is, we need to understand and consider performance over time for programs of both invasive and non-invasive tests.

National Cancer Institute

Budget Caps, FY 2014 and Beyond

CAPS ON DISCRETIONARY SPENDING Budget Authority in Billions of Dollars



A chart of NCI's budget trajectory presented to CTAC. Source: NCI

Federal Funding

NCI's Bills Could Overtake Budget Increases Altogether

(Continued from page 1)

"I want to assure you that I'm not inherently pessimistic—but when you work in budget, as I do, there's just not a lot of room for optimism these days," said Patrick McGarey, the director of NCI's Office of Budget and Finance. "Those increased costs have to be paid first."

For FY2015, the budget is projected to remain essentially flat—that is, a 0.2 percent increase, or a meager \$7.9 million, McGarey said at a March 12 meeting of the NCI Clinical Trials Advisory Committee.

"And \$8 million doesn't go far, I can assure you, in a \$5-billion enterprise," he said.

"It does lay out, I think very effectively, the challenges going forward," said committee chair James Abbruzzese, chief of the division of medical oncology at Duke University Medical Center. "Despite small amounts in increased dollars, a lot of these increased dollars are used up by purposes that are not necessarily programmatic in terms of clinical research, translational research, etc."

If the budget remains flat, rising infrastructure

costs will eat up any modest funding increases under a certain level, and then some.

"For FY15, if we end up with a budget that's 0.2 percent [more], you can expect that programs will be in the negative, unfortunately—because our infrastructure costs will certainly be above that," said McGarey.

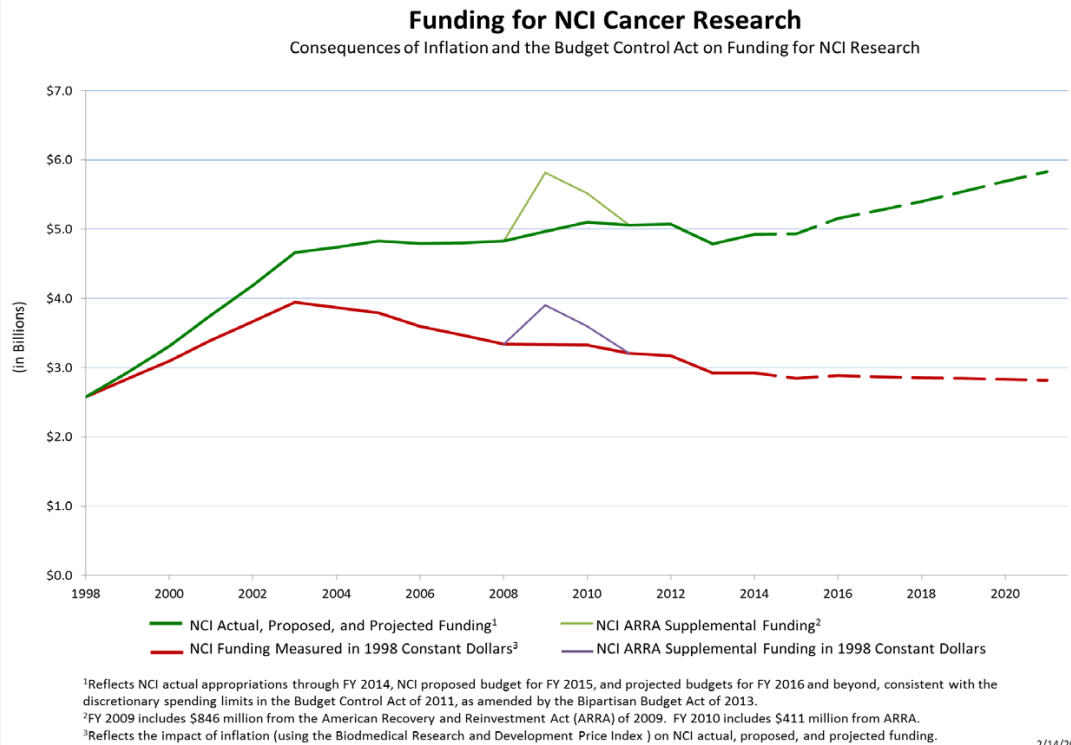
Add in the previous sequester cuts, and it becomes even harder for NCI's budget to return to its previous pace, which even then was falling behind inflation.

"If the NIH does not get more than a 1 percent increase in its appropriation, then we have to make cuts to cover the infrastructure costs that occurred before sequester was ever implemented," said James Doroshov, director of the NCI Division of Cancer Treatment and Diagnosis.

"You're right, that happens every year," replied McGarey. "It's not unique to sequester, but when we don't return to where we were before the sequester, it makes it doubly hard to pay the infrastructure costs, leaving fewer dollars to deserving programs at NCI."

Fighting Escalating Costs and Increasing Inflation

"The growth in rental costs in very recent years around the Washington, D.C., area, especially tight-in with Bethesda [Md.], is significant, and we pay rising costs for rent through a complex arrangement with the [General

Cancer Research Funding, March 2014 *Update*

Services Administration],” McGarey said. “It also includes telecommunications and security requirements.

“I don’t know whether there will be a pay raise. After successive years of no pay raises for federal employees there was a 1 percent [increase] last year,” he said. “There’s a small pay raise in the coming [2015] budget—I don’t know if Congress will approve that—but that alone would more than absorb the 0.1 percent [budget increase]. So you can sort of see how that’s not very encouraging.”

The 2.8 percent increase for 2014 does not represent a change to the long term trend. A chart from the CBO and the House Budget Committee illustrates the temporary bump, which levels out in FY2015.

“It’s a temporary, two-year increase,” he said. “It gave us important and meaningful temporary relief, but it’s not a permanent change.”

In the projected FY2015 budget, the entire federal government will receive a 0.1 percent increase in the aggregate. “NCI did marginally better than that, at 0.2 percent,” said McGarey. “We are slightly favored, but it’s no reason to do anything that resembles popping a champagne cork.”

However, when compared to other institutes and centers at NIH, NCI is receiving a smaller proportion of the \$211 million NIH budget increase, despite making up a larger percentage of the overall budget. According to [a budget brief for 2015](#) produced by the Department of Health and Human Services, NCI’s \$4.9 billion accounts for approximately 16 percent of the total NIH budget, but their additional \$8 million only represents about 3.8 percent of the total increase.

McGarey pointed out that there has been growth in this post-sequester budget climate, but it has often been less than inflation. In looking over the history of the institute’s budget over the past 15 years, NCI’s purchasing power has eroded by 40 percent.

“In 2014, we are below—in real, inflation-adjusted levels—where we were in 1999,” said McGarey.

“Today, if you looked at our budget, it is nominally \$5 billion—but real spending power is only at \$3 billion,” had budget been kept current with the rate of inflation in the Biomedical Research and Development Price Index, he said.

On March 13, the American Association for Cancer Research held a Congressional briefing to

unveil the society's [2013 Cancer Progress Report](#).

"It is an extraordinarily exciting time for cancer research, but the sad and, indeed, frustrating reality is that our ability to deliver the promise of science to patients is in great jeopardy," said Margaret Foti, CEO of AACR. "Despite the \$1 billion in funds that were restored to the NIH and NCI in January, these agencies' budgets remain far below what they were in fiscal year 2012 because of sequestration."

In a March 4 statement, Clifford Hudis, president of the American Society of Clinical Oncology, lamented the requested increases to NIH and NCI's 2015 budgets. "The essentially flat funding (when adjusted for inflation) for the important biomedical research conducted by NIH limits our chances to take full advantage of the exciting scientific advances that promise to save and extend the lives of cancer patients," he said. "ASCO is deeply concerned about continued stagnation of federal research funding and sustained attacks on the nation's cancer care delivery system. Continuing on this path jeopardizes quality and access to care for patients with cancer across the U.S.—and slows the tremendous progress made possible by our nation's historic leadership in science and medicine.

"The President's budget will force new cuts in clinical trials programs and will further strain practices already being forced to shift patients to hospitals and other settings for their chemotherapy. Not only will the nation lose out on unprecedented scientific opportunity before us, we will further compromise the very system we depend upon to deliver the fruits of our research.

"Our patients deserve better."

In Brief

Arthur Caplan to Receive NSB Public Service Award

(Continued from page 1)

He has long been considered an expert in ethical questions that accompany scientific and technological advances. NSB's Public Service Award honors an individual's exemplary service in fostering public understanding of science and engineering.

He is a fellow of the Hastings Center, the NY Academy of Medicine, the College of Physicians of Philadelphia, the American College of Legal Medicine and the American Association for the Advancement of Science.

Caplan is the author or editor of 32 books and over 600 papers in peer reviewed journals. He has chaired a number of national and international committees including the NCI Biobanking Ethics Working Group and the Advisory Committee to the United Nations on Human Cloning, among others.

He writes a column on bioethics for NBC.com, is a commentator on bioethics and health care issues for WebMD/Medscape, and a regular commentator on medicine and science for WGBH radio in Boston.

Among Caplan's many recognitions are the McGovern Medal of the American Medical Writers Association, the Patricia Price Browne Prize in Biomedical Ethics, and a Person of the Year-2001 from USA Today. NSB will present Caplan the award May 6, during the National Science Foundation/NSB Annual Awards Ceremony in Washington D.C.

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VICTOR FAZIO and **HAGOP KANTARJIAN** will each receive lifetime achievement awards from **Castle Connolly Medical Ltd.** during their **National Physician of the Year Awards**, scheduled March 31 in New York City.

Fazio is chairman emeritus of the Digestive Disease Institute at the Cleveland Clinic. Kantarjian is professor and chair of leukemia at MD Anderson Cancer Center.

Fazio's clinical interests are Crohn's disease and ulcerative colitis, colorectal cancer, and pelvic floor reservoir procedures for ulcerative colitis and familial polyposis. He helped pioneer the use of techniques that allow patients to avoid the need for colostomies.

In 2000, he was the first recipient of The Cleveland Clinic Master Clinician Award, given to one of 1,500 Cleveland Clinic physicians. He was selected to be the Rupert B. Turnbull, Jr., MD, Chair in 1995.

On the MD Anderson faculty since 1983, Kantarjian also holds the Kelcie Margaret Kana Research Chair and serves as associate vice president of MD Anderson's Global Academic Programs. He was recently appointed as the Baker Institute Scholar in Health Policy.

Kantarjian has helped develop and demonstrate a number of major treatments, including chemotherapy combinations and the single agent clofarabine for acute lymphocytic leukemia, the hypomethylating agent decitabine, liposomal vincristine for ALL, and ruxolitinib for myelofibrosis.

KENNETH PIENTA was named director of the Prostate Cancer Program at the Johns Hopkins Sidney Kimmel Comprehensive Cancer Center. He is joined by two co-directors, **Samuel Denmeade** and **Shawn Lupold**.

Pienta is a professor of urology and oncology and the director of Urology Research Laboratories in the Brady Urological Institute. He previously held positions as director of urologic oncology and associate dean for clinical and translational research at the University of Michigan Medical School.

Denmeade will continue his translational research efforts conducting innovative clinical trials through his clinical practice and developing new therapeutics in the lab. He is a professor of oncology, pharmacology and molecular sciences, and urology, and has collaborative relationships with colleagues across the institution and mentors fellows and young investigators in the Department of Oncology.

Lupold is an associate professor of urology,

oncology and radiation oncology and molecular Radiation Sciences and his research focuses on prostate cancer biology with the goal of exploiting prostate and cancer tissue-specificity to develop new diagnostic, prognostic, and therapeutic agents.

THE AMERICAN SOCIETY OF HEMATOLOGY announced 15 research investigators who will receive critical interim support for hematology research proposals that, despite earning high scores, could not be funded by the NIH amid severe funding reductions.

The support will come in the form of one-year, \$100,000 Bridge Grants, awards intended to help bridge these talented ASH member investigators to their next NIH research grant by funding efforts to gather additional data to strengthen the resubmission of their applications.

The 15 recipients join 29 hematologists that have been granted funding since ASH created the program in July 2012, nearly one-third of which have already successfully obtained NIH funding.

The March 2014 awardees are:

- **Joel Bennett**, University of Pennsylvania
- **John Conboy**, Lawrence Berkeley National Laboratory
- **John Cowell**, Georgia Regents University
- **Adam Goldfarb**, University of Virginia
- **Jordan Jacobelli**, National Jewish Health
- **Michael Jordan**, Cincinnati Children's Hospital
- **Neil Kay**, Mayo Clinic
- **Jatinder Lamba**, University of Minnesota
- **Keith McCrae**, Cleveland Clinic Foundation
- **Joanne Murphy-Ullrich**, University of Alabama at Birmingham
- **Elizabetha Nemeth**, UCLA
- **Trista North**, Beth Israel Deaconess Medical Center
- **Alvin Schmaier**, Case Western Reserve University
- **Demin Wang**, BloodCenter of Wisconsin
- **Don Wojchowski**, Maine Medical Center Research Institute and Tufts University School of Medicine

F. MARC STEWART was named incoming president of the board of directors of both the **Patient Advocate Foundation** and **National Patient Advocate Foundation**.

Stewart has been a member of the foundation's scientific board since 2003. Since 2000, he has been a professor of medical oncology at the University of Washington Medical School, medical director for the Seattle Cancer Care Alliance and a member of

the Fred Hutchinson Cancer Research Center. He also serves on the editorial board for the Journal of Cellular Biochemistry and the Journal of Intensive Care Medicine.

The foundation is a national non-profit that seeks to safeguard patients through effective mediation, assuring access to care, maintenance of employment, and preservation of their financial stability by providing professional case management services to individuals facing barriers to healthcare access. According to the foundation, they helped resolve 109,147 cases for patients that required mediation and arbitration services in 2012.

THE OHIO STATE UNIVERSITY signed a licensing agreement with **MedVax Technologies Inc.**, for the licensing of cancer peptide vaccine technologies.

The vaccines are designed for the treatment and prevention of cancers associated with the HER2 protein, including breast, ovarian, lung, colon and pancreatic cancers, and gastrointestinal stromal tumors. The commitment by MedVax will allow clinical trials for various cancers to be conducted in the near future.

Development of these technologies follows decades of research led by Pravin Kaumaya, a cancer researcher with The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital & Richard J. Solove Research Institute Innate Immunity Program.

The work has been funded by nearly \$15 million in grants from NCI and NIH (grants CA 84356, CA 094555, CA 135608, CA 82869). Additional funding was provided by Pelotonia and Fore Cancer Research.

THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO signed an agreement with **Advaxis Inc.** to evaluate several new immunotherapy constructs, each built on Advaxis proprietary technology.

One construct, ADXS-PSA, is an immunotherapy that is designed to target the PSA antigen associated with prostate cancer. By incorporating PSA into the Advaxis live, attenuated vector, researchers intend to deliver the PSA antigen, fused to the powerful immunostimulant LLO, directly inside antigen presenting cells that are capable of driving a cellular immune response to PSA expressing cells. The approach is also designed to inhibit the Treg and MDSC cells that contribute to immunologic tolerance of prostate cancer.

UCSF researchers have identified several tumor targets associated with clinical responses in immunotherapy studies for prostate cancer and will

collaborate with Advaxis scientists to adapt these targets to the Advaxis immunotherapy platform. Researchers plan to advance ADXS-PSA to phase I trials in the first half of 2014.

ADXS-HPV, for the treatment of HPV-associated cancers, has demonstrated improved survival and objective tumor responses in a phase II trial in 110 patients with recurrent cervical cancer. ADXS-HPV is also being evaluated in other HPV-associated cancers including a phase II in advanced cervical cancer, a phase I/II in head and neck cancer, and a phase I/II in anal cancer. ADXS-HPV has orphan drug status for both anal and head and neck cancers.

Advaxis has created more than 20 distinct immunotherapies based on its platform, and also has clinical research collaborations with the University of Pennsylvania, Brown University, the Georgia Regents University Cancer Center, the Icahn School of Medicine at Mount Sinai, among others.

GEORGIA REGENTS MEDICAL CENTER received the **CEO Cancer Gold Standard** accreditation from The CEO Roundtable on Cancer.

The nonprofit organization of CEOs, founded by former President George H.W. Bush, created the accreditation in collaboration with NCI, many of its designated cancer centers, and other leading health organizations, which requires companies to evaluate their health benefits and corporate culture and take extensive, concrete actions in five key areas of health and wellness to reduce the risk of cancer in the workplace.

To earn Gold Standard accreditation, a company must establish programs to reduce cancer risk by discouraging tobacco use; encouraging physical activity; promoting healthy diet and nutrition; detecting cancer at its earliest stages; and providing access to quality care, including participation in clinical trials.

In addition to NCI and the Centers for Disease Control and Prevention, 16 NCI-designated cancer centers and more than 60 other hospitals have earned the accreditation.

THE RESEARCH!AMERICA Advocacy Awards was held March 12 in Washington, D.C., recognizing individuals and organizations are those whose leadership efforts have been notably effective in advancing our nation's commitment to research.

The Edwin C. Whitehead Award for Medical Research Advocacy was awarded to **Reps. Frank Wolf (R-Va.)** and **Chaka Fattah (D-Penn.)**, for their commitment to supporting policies that promote federal

and private sector medical research and innovation.

Wolf is currently a senior member of the House Appropriations Committee, presides as chairman of the Commerce, Justice, Science Subcommittee, and is a member of the Transportation, Housing and Urban Development and State and Foreign Operations subcommittees. He founded a commission to bolster federal science, technology, engineering and mathematics education programs.

Fattah is an advocate for research and innovation as the ranking member of the Appropriation Committee's Commerce, Justice, Science and Related Agencies subcommittee. He leads the Fattah Neuroscience Initiative, an interagency approach to to significantly increase federal investment in neuroscience research.

Glenn Close, the award-winning actress of *Damages* and *Fatal Attraction*, will be honored with the Isadore Rosenfeld Award for Impact on Public Opinion.

Close co-founded Bring Change 2 Mind, a not-for-profit organization dedicated to ending the stigmas and misunderstandings surrounding mental illness. She blogs about her personal experiences on the BC2M website and has written two books, *The Warping of AI* and the soon-to-be-released memoir, *Resilience*.

The Raymond and Beverly Sackler Award for Sustained National Leadership was presented to **Reed Tuckson**, managing director of Tuckson Health Connections, for advocating the benefits of evidence-based medicine to the public and policymakers. As executive vice president and chief of medical affairs at UnitedHealth Group, he embraced data analysis and mobile technologies, pioneering new digital delivery systems for evaluating care and collecting data.

The Progeria Research Foundation will receive the Paul G. Rogers Distinguished Organization Advocacy Award. PRF helped secured language in the Children's Health Act of 2000 in support of rare disease research, including progeria. The organization also led the discovery of the progeria gene, the identification of a potential drug treatment and, eventually, the first progeria clinical trial which resulted in the first treatment of the disease.

The Gordon and Llura Gund Leadership Award was presented to **Kathy Giusti**, founder and CEO of the Multiple Myeloma Research Foundation, for advancing the research and treatment of myeloma. The organization established the first myeloma tissue bank and launched an initiative that resulted in the complete mapping of the myeloma genome, which was made publicly available to advance myeloma research.

The Geoffrey Beene Builders of Science

Award was presented to **Leroy Hood**, for developing instruments that allowed the successful mapping of the human genome.

Hood was one of a small number of early and persistent advocates for the Human Genome Project. Prior to his invention of the automated DNA sequencer, it took 30 years to sequence the genome of the cold virus, and the first gene cost \$180 million to sequence. Afterwards, it took less than a day to sequence the genome of the SARS virus and the cost of sequencing a gene is now \$6. Hood received the National Medal of Science from President Barack Obama in 2013, one of the nation's highest scientific achievements.

The European Commission approved a subcutaneous formulation of MabThera (rituximab) for the treatment of patients with follicular lymphoma and diffuse large B-cell lymphoma.

Following the approval of Herceptin SC in September 2013, this is the second European approval for a novel subcutaneous formulation of one of Roche's oncology products using Halozyme's patented Enhance (recombinant human hyaluronidase) technology.

The European approval was primarily based on data from the pivotal SABRINA study, which was recently published in the *Lancet Oncology*. Roche has stated that they expect to begin launching MabThera SC in a number of European markets throughout 2014.

The Japan Ministry of Health, Labor and Welfare granted approval to the Lonsurf combination tablet T15 and T20 (trifluridine and tipiracil hydrochloride), for the treatment of patients with unresectable advanced or recurrent colorectal cancer, if refractory to standard therapies.

Japan is the first country in the world to grant marketing authorization for Lonsurf, according to Taiho Pharmaceutical Company Ltd., the drugs' sponsor. The approval is based primarily on the results of a randomized, double blind placebo controlled phase II clinical trial conducted in Japan (J003-10040030). Taiho is conducting a global phase III clinical trial, named RECURSE, on patients with metastatic colorectal cancer refractory to standard chemotherapies.

Lonsurf is a combination drug of trifluridine and tipiracil hydrochloride. Trifluridine is an antineoplastic nucleoside analog, which is incorporated directly into DNA, thereby interfering with the function of DNA. Its blood concentration is maintained via tipiracil hydrochloride.