THE CANCER LETTER

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Medicare Cuts

Cuts Claimed to Displace "Millions" of Patients Yet None Seem to Complain. Why Not?

By Paul Goldberg

Earlier this month, as sequestration cuts in Medicare started to take effect, The Washington Post reported that payment reductions are prompting office-based oncology clinics to "turn away" thousands of Medicare patients.

This shocking news report—in conjunction with lobbying by oncology organizations—apparently persuaded Congress to produce a bill called the Cancer Patient Protection Act of 2013.

Introduced by Rep. Renee Ellmers (R-N.C.), the bill—HR 1416—seeks to repeal sequestration as it affects drugs and biologicals administered by office-based physicians to cancer patients, directing Medicare to pay back any reduced payments made since the cuts took effect April 1. At this writing, the bill has 43 co-sponsors.

The Post story is also cited in a letter to the Centers for Medicare and Medicaid Services, in which 124 House members expressed concern that Medicare cuts are forcing oncologists to turn away cancer patients.

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Sequestration

NCI Seeks to Maintain Grant Success Rate As Budget Deadlock Deepens on Capitol Hill

By Matthew Bin Han Ong

As pressure to eliminate sequestration continues to mount, President Barack Obama announced support for a Senate proposal April 24 to cancel out the 5.1 percent across-the-board cuts by drawing funds from the budget for the global war on terrorism.

The program, formally known as Overseas Contingency Operations, pays for military operations in Iraq and Afghanistan and other national security goals abroad, which includes support for a civilian-led government in Iraq.

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In Brief

ASCO Defines Clinically Meaningful Outcomes

THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY issued draft recommendations that offer minimum standards for the design of clinical trials.

The recommendations—developed by the ASCO Cancer Research Committee—propose a minimum increase in overall survival that should be

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Counselors, Call Centers Receive No Complaints From Patients

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"As an unintended consequence of sequestration, millions of Americans are facing delayed care for life-saving treatments," Ellmers said in a statement as she introduced the bill.

If indeed millions—or, as per account in The Washington Post, thousands—of cancer patients are being referred out by their doctors, one would expect to encounter complaints and protests from these patients and their families.

Yet, surprisingly, nearly a month after sequestration cuts to Medicare went into effect, neither patients nor their families seem to have much to say about the change.

The call centers at the American Cancer Society usually get a million phone calls and 23 million emails a year, but over the past month they received no calls or emails about this problem.

"We've heard nothing to speak of at our local offices or at our nationwide call center," an ACS spokesman said to The Cancer Letter.

Similarly, the Cancer Support Community is well positioned to detect problems in cancer care in the U.S. The group is focused on providing direct psychosocial support to cancer patients, serving over 80,000 people a year through its 150 counseling centers, an online support network and a telephone help line.

"We knew when there were issues with drug shortages," said Linda House, executive vice president of external affairs for the organization. "We deal with social and emotional distress, and we had people coming in who were distressed because they were unable to get a particular generic drug. But we are not seeing anything of the sort yet.

"As of a week-and-a-half ago, we had not received any patient come in and say they were denied care as a result of sequestration. We will continue to monitor this closely."

The National Breast Cancer Coalition, an umbrella group of breast cancer organizations which fervently keeps tabs on the quality of care issues, hasn't gauged anything either. "We have not heard from our members that this is a problem," said NBCC President Fran Visco.

Defining the Problem

Could it be that the very patients, in whose name the change is being proposed, are not affected by the Medicare cuts?

And if they are, why are they so silent?

"Before we can rationally address a problem, we need to make sure the problem is defined in a manner supported by facts," said Bob Erwin, president of the Marti Nelson Cancer Foundation. "The facts do not seem to support the idea that this is a patient access problem.

"If the real issue is the impact of sequestration on small oncology practices, that could be important to address, but it is not a problem of access and can only be addressed effectively if it is done accurately."

For office-based oncology practices, the effect of sequestration could be considerable.

Since the CMS is applying the sequestration cut both to payments for Part B drugs and to the 6 percent services payment, the result, after accounting for patient copayments, will be to cut reimbursement to ASP plus 4.3 percent.

In the President's budget proposal for fiscal 2014, payment would be further reduced to ASP plus 3 percent.

This is occurring at a time when an increasing number of office-based oncology practices are either closing doors or—more commonly—selling to hospitals, which are able to charge higher rates, obtain drugs at more significant discounts and write off uncollected debts.

"Community oncology practices that are heavily reliant on Medicare to insure their patients are likely the providers with the most to lose in practice revenue because of sequestration," said Rena Conti, an economist and assistant professor of hematology and oncology at the University of Chicago Department of Pediatrics.

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"This is because a practices' acquisition costs for Part B drugs are a function of how much bargaining power they hold to obtain discounts and rebates off [wholesale acquisition cost] from wholesalers," Conti said. "The majority of physician practices and hospitals with high volumes or who are members of group purchasing organizations have the greatest ability to obtain such discounts off list price and therefore maximize their revenue on the use of these drugs."

Also, some oncology practices and hospital-operated centers are able to purchase drugs under discounts available through the 340B program, which makes drugs available at discounts of 30 to 50 percent off list price.

Conti and colleague Peter Bach, of Memorial Sloan Kettering Cancer Center, recently published a piece in the Journal of the American Medical Association examining how the 340B program creates financial windfalls, which primarily benefit hospitals and large practices.

Patient Care Uninterrupted

The Post story about thousands of displaced cancer patients has been reverberating throughout the U.S.

Local news outlets are attempting to run something similar, to gauge whether an oncology practice around the corner is telling Medicare patients to go away.

Talking with the Salt Lake Tribune, Richard Frame, a medical oncologist at Utah Cancer Specialists, said that his large practice has referred 10 Medicare patients to hospitals and has identified 100 more for possible transfer.

"We're being pushed off the cliff," Frame said to the local newspaper. "Inconvenient is not the right word for it. It's tragic when you have patients you've been treating in your office and now all of a sudden you have to arrange to have them treated elsewhere."

The Cancer Letter sent Frame an email asking for specifics on the sort of patients who were being referred out, but he looped in an employee of Community Oncology Alliance, a lobbying group, and didn't address the questions.

John Ruckdeschel, medical director of the Oncology Clinical Program at Intermountain Healthcare, who sees patients through Utah Cancer Specialists, was able to shed light on the situation in the state. Ruckdeschel's patients seem to be thoroughly protected from any adverse consequences of being shifted from a private practice to a hospital.

Ruckdeschel sees patients in the UCS office on the second floor of the Intermountain Cancer Center in Murray, Utah, in the Salt Lake City area.

If his patient's insurance covers the costs associated with chemotherapy, including the drugs, the patient is sent to an infusion area a couple of doors down the hall, at the private practice.

If the patient's insurance does not cover the costs, or if the patient has no insurance, the patient has to get in an elevator and travel one floor up, to Intermountain's Infusion Service.

The doctor doesn't change. It's Ruckdeschel.

"I don't think being assigned to one infusion area or another makes a difference to the patients," he said.

"There is nothing new about sending patients whose insurance does not cover the costs of treatment to a hospital based infusion center.

"This has been going on for decades, through most of my career. What's different is that numbers of patients referred have increased, because now a major payer, Medicare, is reducing its reimbursement. What was a fairly delicate balance between expense and revenue has been tipped off-balance.

"It's increasing the number of people who get referred to hospital-based clinics, but it is not people being sent out into the street to die," Ruckdeschel said.

At the Intermountain infusion center, patients can be infused with drugs obtained through the 340B discount program.

While patients at Ruckdeschel's office would hardly notice being referred to a hospital, in other settings it may involve a move to another facility or even another oncologist.

Deciding Whom to Refer

The decisions on referring out Medicare patients likely differ from practice to practice.

At the Northwest Georgia Oncology Centers, a practice that employs 21 physicians at 10 locations, about 70 patients have been referred to local hospitals' outpatient departments.

"It's more than we want, but it's a small percentage of our overall Medicare population," said Scott Parker, the practice's executive director. "That's probably around 1 percent."

Scott said that the practice has able to treat almost all patients, but after sequestration, it identified "eight or nine" regimens where the practice was unable to cover the cost of the drug.

"If, strictly from cash flow standpoint, the administration services aren't even covering the cost of our drugs, then we shift those to the hospital outpatient setting," Parker said. "And, keep in mind, we are

actually including the chemotherapy administration. We add that to our analysis, and if the administration reimbursement still doesn't cover the costs of the drug, we just cannot do it in the office.

"As long as sequestration is in effect, as we get new patients that we are going to be totally underwater on, we are going to send those to the hospital outpatient departments, too."

The treatments that become not feasible would likely vary from practice to practice, depending on drug purchasing arrangements and costs.

Some of the patients who were referred to the hospitals now have to travel longer distances to get care, Parker said.

"I believe, at six of our locations the patients have to drive on average about 20 miles one way to a hospital system that has an outpatient department," he said. "And then the other issue, there have been some treatment delays. We've not had any patients who were on treatment whose treatment has stopped. They are being inconvenienced with additional drive time, and they may be inconvenienced with the additional wait, but they are still being treated."

House Letter Seeks Information from CMS

In a letter to CMS, 124 House members seek to clarify the agency's authority to implement the sequestration cuts and ask for data on impact of the cuts on patients' access to care.

The letter to Acting Administrator Marilyn Tavenner was led by Reps. Pete Sessions (R-Tex.), Gene Green (D-Tex.), Mike Burgess (R-Tex.), Allyson Schwartz (D-Penn.), Ed Whitfield (R-Ky.) and Ron Kind (D-Wisc.), asks CMS to use its authority to apply the 2 percent sequester cut to only the service payment and not to the cost of chemotherapy drugs and biologic treatments.

The text of the letter follows:

Dear Acting Administrator Tavenner:

We write regarding the two percent sequestration reduction to Medicare payments to providers—particularly those caring for cancer patients—effective April 1, 2013. We are concerned about how this cut will be implemented and if there is any flexibility available to your agency in how the cut is applied to the payments. Unencumbered access to critical cancer medicines for Medicare beneficiaries is a top priority for us and we would like to work with you to find a path forward that does not result in cancer patients being turned away by their oncologists.

As you know, the Medicare Modernization Act of 2003 (MMA) changed the pricing for cancer drugs covered under Medicare Part B to Average Sale Price (ASP) plus six percent. The intent was to reimburse cancer clinics and other providers for their drug acquisition costs at average market rates and to include an additional services payment (i.e., 6%) to cover inventory, facilities, storage, handling and waste disposal costs.

Our concerns are two-fold. First, it is unclear to us if the Centers for Medicare and Medicaid Services (CMS) has the statutory authority to reduce Medicare Part B drug reimbursement since the amount is specified in the MMA. Second, concerning sequestration, the Office of Management and Budget (OMB) has issued

guidance instructing federal agencies and departments to, "[u]se any available flexibility to reduce operational risks and minimize impacts on the agency's core mission in service of the American people…"

Per a March 1, 2013, OMB memorandum notifying all federal departments and agencies of the sequestration order, "Agencies should operate in a manner that is consistent with guidance provided by OMB in Memorandum 13-03..." We would like to see CMS use any flexibility that exists to implement the cuts in such a way that the core mission of the agency—to provide care to beneficiaries—is retained and protected.

It was reported in the news that cancer clinics across the country are already turning away thousands of Medicare patients advising them to seek treatment elsewhere, citing the Medicare sequester cuts that took effect April 1. Our hope is that there is a solution that neither diminishes the access of beneficiaries to the treatments they need nor their ability to seek needed treatment in the setting of their choice. We would like more information on this issue from CMS and request your help in addressing the following:

1. Are Medicare Part B drug reimbursement rates set in statute?

2. Does CMS have, and if so, intend to use the authority to reduce Medicare Part B drug reimbursements?

3. Will CMS be monitoring access to care for Medicare beneficiaries once the sequester takes effect—particularly for services where interruption or delay could mean success or failure of treatment, such as cancer care? What steps has CMS taken to avoid negatively affecting Medicare beneficiaries receiving chemotherapy and other specialty infusible drugs?

4. Does CMS believe any flexibility exists to modify cuts in areas where access barriers become present?

5. How will CMS calculate the reduction required under the sequester? Will it apply to the entire payment for the drug (ASP+6%) or only the base ASP amount, or only to the +6%?

6. Has CMS reviewed the potential program costs and impact on Medicare beneficiaries that the reduction required by the sequester may cause? For example, will reduced access to cancer clinics cause beneficiaries to seek services in higher-cost sites of care?

7. Have you received or collected any information about Medicare beneficiaries, to date, being turned away from their healthcare provider due to uncertainty about the future reimbursement rates for their Part B drugs?

We ask that you answer the questions posed and if ultimately this cut is applied, use any and all flexibility available to you to ensure a potential sequester cut is applied to just the 6 percent service payment and not to the underlying fixed drug cost (ASP). We are asking, therefore, that any available flexibility be used to direct the cuts away from patients. Our hope is that there is a solution that protects patients' access to their healthcare professionals. We look forward to working with you to implement impending spending reductions in a way that does not threaten needed access to care for Medicare beneficiaries.

Thank you again for your attention to this important matter. In light of the sequester implementation on April 1, we kindly request that you provide a response to this letter on or before April 29, 2013.

Sequestration

NCI Seeks to Maintain Grants Under Heavy Budget Pressure

(Continued from page 1)

A brainchild of Senate Majority Leader Harry Reid (D-Nev.), the proposal would postpone the $85.3 billion sequestration cut for the next five months by borrowing from the OCO's budget, which is capped at $450 billion through 2021. Next year's dollar amount has not been determined due to delayed decisions about troop levels.

"I think we should do something about sequestration," Reid said April 23. "We should do what was in one of the Ryan budgets; that is, use the Overseas Contingency Fund to delay the implementation of sequestration."

In a statement issued by his office, Rep. Paul Ryan (R-Wis.) denied having endorsed the idea.

The renewed Congressional fervor to end sequestration came after 47,000 Federal Aviation Administration employees were furloughed April 21, causing 1,200 flight delays nationwide over the following 48 hours.

Senate members took to the floor Tuesday to protest the delays; GOP lawmakers blamed the Obama administration for failing to prioritize and avoid impact to aviation. Earlier this month, Republicans also criticized the president for sensationalizing the cuts because they claimed no pain was felt when sequestration went into effect.

Talk of a grand bargain is, once again, going nowhere on Capitol Hill—Senate Republicans earlier this week blocked Democratic attempts at setting up a budget conference with the House of Representatives.

Also, budget differences between all three parties continue to plague negotiations:

The White House insists on more than $1 trillion in tax revenue. The Senate proposes to reverse sequestration through cuts to defense programs and non-discretionary programs. And the House wants to roll back the defense cuts and repeal the Affordable Care Act.

Both chambers of Congress formally rejected the other's plan before the end of March, while the President's budget proposal received no support from Republicans and only a lukewarm response from Democrats.

Having held two dinners with Senate Republicans this week following a Q&A session with House Republicans in March, Obama appears to be reaching across the aisle in his second term.

The president's top aides met with Senate Republicans April 25 in an attempt to forge a coalition and strike a budget deal before the country reaches the debt ceiling, around May 19.

NCI Goal: Maintain Grant Success Rate Without Layoffs

Despite sequestration, NCI will try to keep the grant success rate at 13 to 14 percent, Director Harold Varmus said April 8 in his talk at the annual meeting of the American Association for Cancer Research.

There will be no staff reductions at the institute, said Varmus.

"This does not mean everything is happy at the NCI—indeed, personnel who work for the government are required to obey stricter restrictions on travel and many other things than you and the outside community would enjoy," Varmus said, as the institute prepares to cut as much as $219 million from its $5 billion budget.

Cuts to NIH add up to $1.486 billion for the remainder of the fiscal year.

"We are going to be maintaining our number of trainees and our training stipends," Varmus said.

The institute has yet to announce how it would precisely manage the cuts.

Though Congressional budgets have not revealed details of the 2014 funding for NIH and NCI, members of the Senate have proposed a bipartisan amendment to create a deficit-neutral reserve fund which would help grow NIH's budget through 2023.

In his AACR remarks, Varmus bemoaned NCI's declining success rates for research grant applications.

"Our community is growing, the cost of research has been rising, the size of grants has not kept up with that increased cost of research, the scientific opportunities have multiplied, and our success rates have been falling," Varmus said.

"The main thing you can see here is the decline in success rates for individuals competing for new research project grants from the mid-20s to about 13 or 14 percent where it has been the last couple of years."

The institute will attempt to issue roughly the same number of grants at about the same funding levels as it has in recent years.

"This is obviously not good, but it's better than falling further," Varmus said. "And we're doing this by trimming basically everything that we can trim—non-competing awards, intramural programs, contracts, many other categories of spending that we have at the NCI."

There are still many scientific opportunities, because the institute's budget is substantial despite the cuts, Varmus said.

"Although we are far from the finish lines with most cancers, the recent successes that you have been hearing about at this meeting, the talented people that populate our scientific laboratories and clinics, and the new opportunities for moving faster against cancer, encourage optimism which I, and I hope many of you, feel," Varmus said. "Lamenting the situation is inescapable, but exploiting new scientific opportunities is crucial. We can't afford to waste these opportunities during the current budgetary squeeze."

Varmus's Remarks at AACR

Varmus's remarks at the AACR annual meeting immediately preceded the Rally for Medical Research, an event that brought together 12,000 people (The Cancer Letter, April 12).

The excerpted text of his remarks follows:

In a few minutes, many of you are going to be heading outside for a Rally for Medical Research, and in this way, you'll remind the larger public about the importance of science for health and tell them about how recent budget cuts affect our ability and your ability to use science to counter illness.

Last week, President Obama used his bully pulpit as another way to highlight for the public the importance the ambitions and the possibilities for science when he proposed the [$100 million] brain initiative.

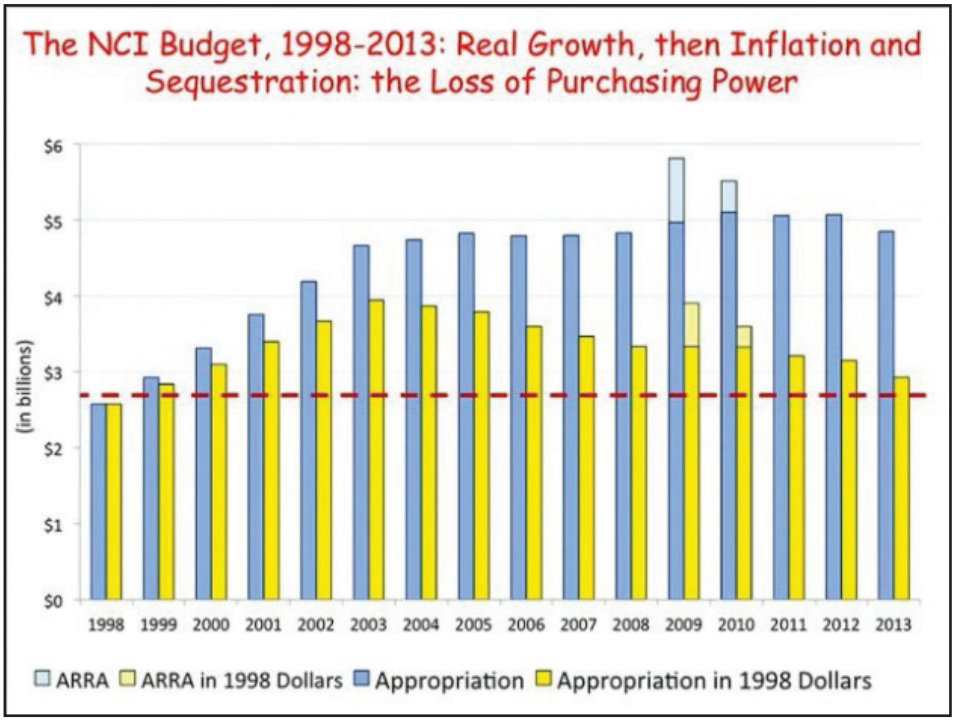
Now these events are good news for the future of science, but they come too late to solve the problems that all of us face—we at the NCI, scientists in this room, scientists dependent on the NCI throughout the U.S. and elsewhere—the difficulties that those scientists are going to face for the rest of this fiscal year, and likely

for a few years to come.

So my job this morning is twofold. First, to tell you how the NCI plans to manage the fiscal situation that is difficult for all of us, and to tell you how we plan to continue to extraordinary scientific progress that you have been hearing about at this meeting.

Lamenting the situation is inescapable, but exploiting new scientific opportunities is crucial.

First, it is important to remember that we have just not fallen over a fiscal cliff. We have been losing spending power and watching declining success rates since 2003. It's just happening a bit faster this year.



The slides that accompanied Varmus's remarks at the AACR annual meeting are available on The Cancer Letter website.

Second, we should remember that NCI still has a budget of about $4.8 billion, and a lot can be done with that.

Third, although we are far from the finish lines with most cancers, the recent successes that you have been hearing about at this meeting, the talented people that populate our scientific laboratories and clinics, and the new opportunities for moving faster against cancer, encourage optimism which I, and I hope many of you, feel.

So we can't afford to waste these opportunities during the current budgetary squeeze.

Finally, we should also remember that we have multiple partners in funding cancer research. It's just the NCI, there are advocacy groups, funding organizations, and many other countries, other U.S. agencies engaged in cancer research, donors at academic centers, collaborators throughout industry.

They help soften, although they can't completely eliminate, the blows conferred by sequestration. Let me tell you, in little more detail, what we are facing as a result of changes in this setting.

So, let me first point out to you the patterns of funding we've been seeing over the last 15 years or so.

Many of us recall the doubling of the NIH budget, but after that, beginning in 2004, the budget has been flat except for a couple of years in which we got much needed and much appreciated additional resources through the recovery act—money that was only given to us over the course of two years.

And since then, the budget has been flat and, just this year, as a consequence of the sequestration, we've lost a little over 5 percent of our budget.

During that time, however, the loss due to inflation has eroded our spending ability and constant dollars to a level that we haven't seen since the year 2000 to 2001. However, having that amount of money or spending power today compared to 2001 is not the same thing.

Our community is growing, the cost of research has been rising, the size of grants has not kept up with that increased cost of research, the scientific opportunities have multiplied, and our success rates have been falling.

The main thing you can see here is the decline in success rates for individuals competing for new research project grants from the mid-20s to about 13 or 14 percent where it has been the last couple of years.

"This is Obviously Not Good"

Let me say a word or two about what we are doing at the NCI to try to manage the sequestration that's going to bring our budget down by a little over 5 percent this year.

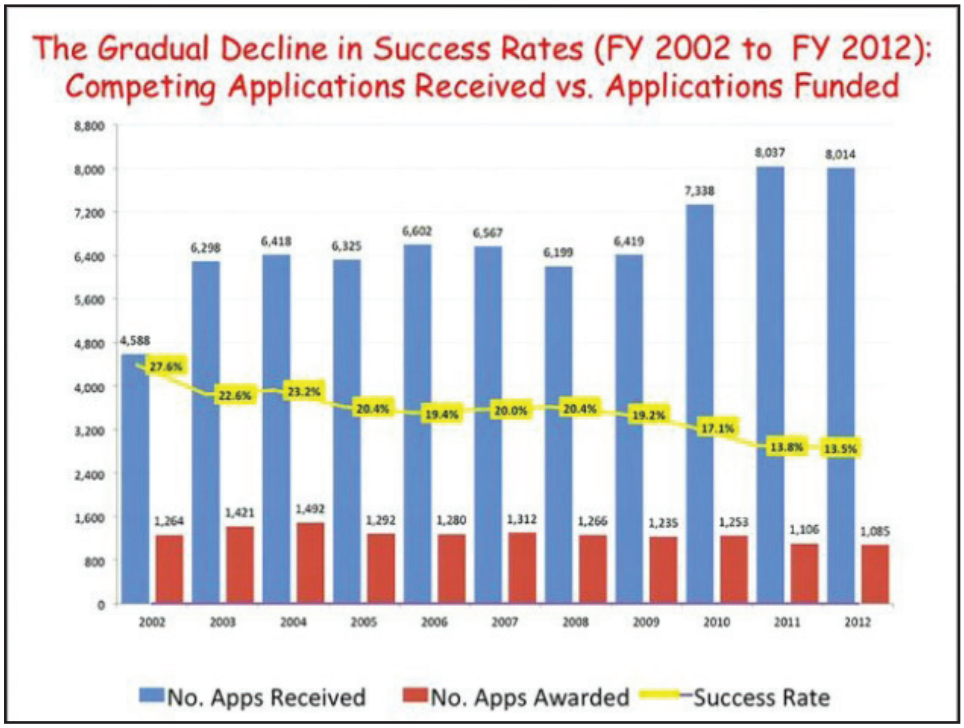
First, we are making every effort to issue roughly the same number of grants at about the same funding levels this year as we have in the last couple of years. That means the success rate will be about 13 to 14

percent.

This is obviously not good, but it's better than falling further. And we're doing this by trimming basically everything that we can trim—non-competing awards, intramural programs, contracts, many other categories of spending that we have at the NCI.

Secondly, we're constrained by departmental policy and that is a happy thing. We're not going to be taking layoffs or reducing the staff.

This does not mean everything is happy at the NCI—indeed, personnel who work for the government are required to obey stricter restrictions on travel and many other things than you and the outside community would enjoy.



Third, we're going to be maintaining our number of trainees and our training stipends.

I can't give you firmer numbers on all these things because unbelievably, partway into April of fiscal year 2013, we still don't have a definite number for our budget for this year, but we plan to continue the current practices that I believe, are important to maintain, especially in this environment—first, to pursue new ideas through initiatives that I will be describing to you in a moment, and it's important that we carefully monitor the way in which we're making grants.

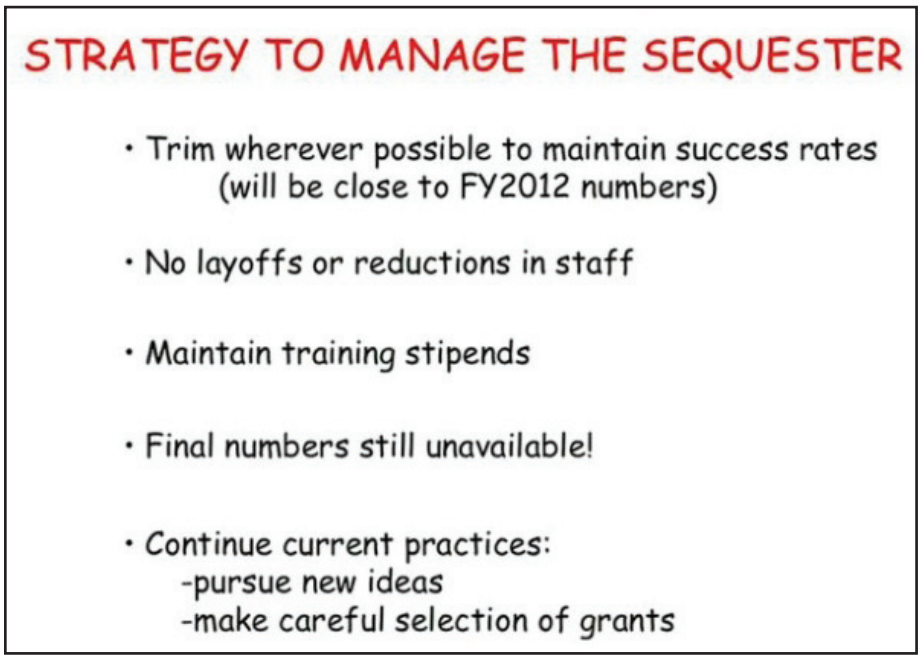
We do not have a simple payline, and as the next slide will show, we have a practice which you can all observe by going to the NCI homepage and finding the information or by using the URL at the bottom of this image.

We have an open system for showing you exactly how different categories of grants fare in the review process—your chances of getting funded are obviously higher the better your score is, but there is no firm payline.

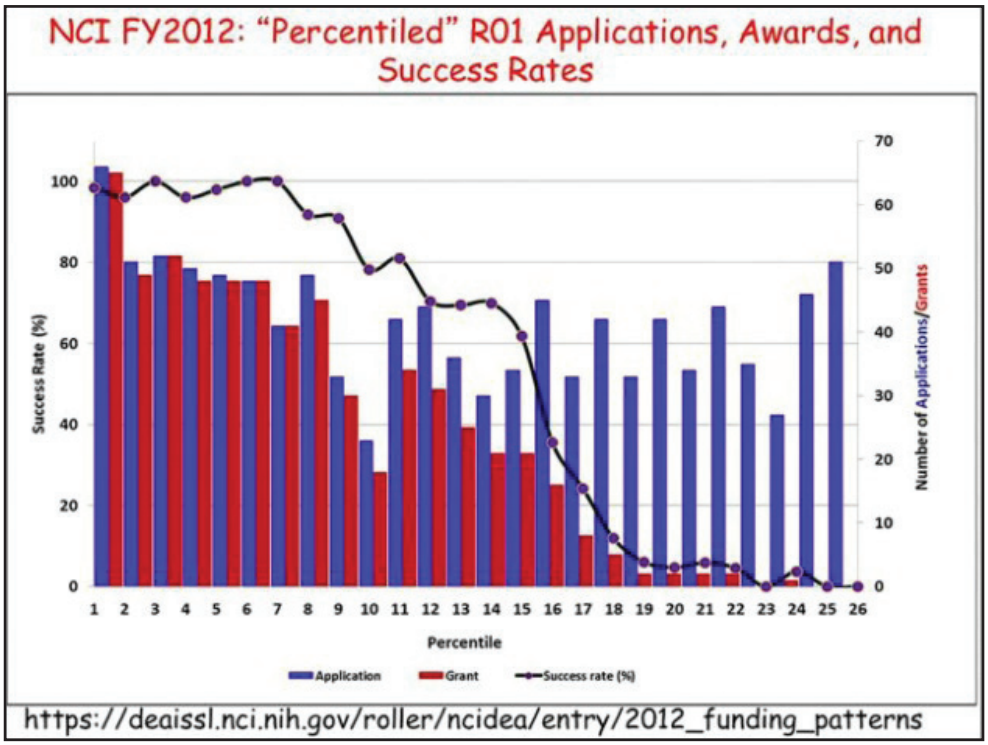
Most applications that receive priority scores are 9 or better, 10 to be funded, but with a few exceptions. After that, as the scores decline, the likelihood of funding declines, and the overall success rate, as I've emphasized, is not, as some has thought, 7 or 9 percent. Overall, success rate is about 13 to 14 percent.

This is not an ideal situation. None of us like it, the amount of funds we provide are not generally adequate to fully fund research.

We have to continue



to think about how we use the funds that are available, because they are considerable, and the public place has a lot of confidence in us to be sure that we use those well, and I'd like to tell you now about how we plan to do that.



NCI's Initiatives Will Go Forward

You've been hearing a lot at this meeting about precision medicine and the importance of using new tools in genomics, informatics and science-based clinical trials to advance our ability to use both drugs and new immunotherapies to better the case for cancer patients.

Many of you, I hope, have seen this simple diagram from the National Research Council's report issued a year and a half ago on precision medicine.

And I want to emphasize here that the one particular characteristic of the circuit, namely the dependence of our ability to use genomic analysis as a means of creating a new taxonomy for cancer for improving our diagnostic ability for improving treatments and outcomes—all that depends very heavily on a knowledge network—a computer-based system for aggregating data from many sources, from clinical treatments, from clinical trials, from medical research generally—into a cancer knowledge commons that all can use.

The NCI and many other organizations are in the process of figuring out the best way to do that.

All of you who are NCI grantees received an email from us a couple of days ago asking you to provide us with ideas and metrics for improving the way in which we carry out the creation of appropriate knowledge networks—we being the NCI in collaboration with many of our partners.

An important source of information for creating a knowledge commons depends on a project you've been hearing much about: the TCGA, the Cancer Genome Atlas, which is also affiliated with the International Cancer Genome Consortium.

This slide presents, in graphic form, the progress being made, which is considerable, on our efforts to characterize, in a range of 500 cancers and abnormal tissue from the same patients, from at least 20 different forms of cancer.

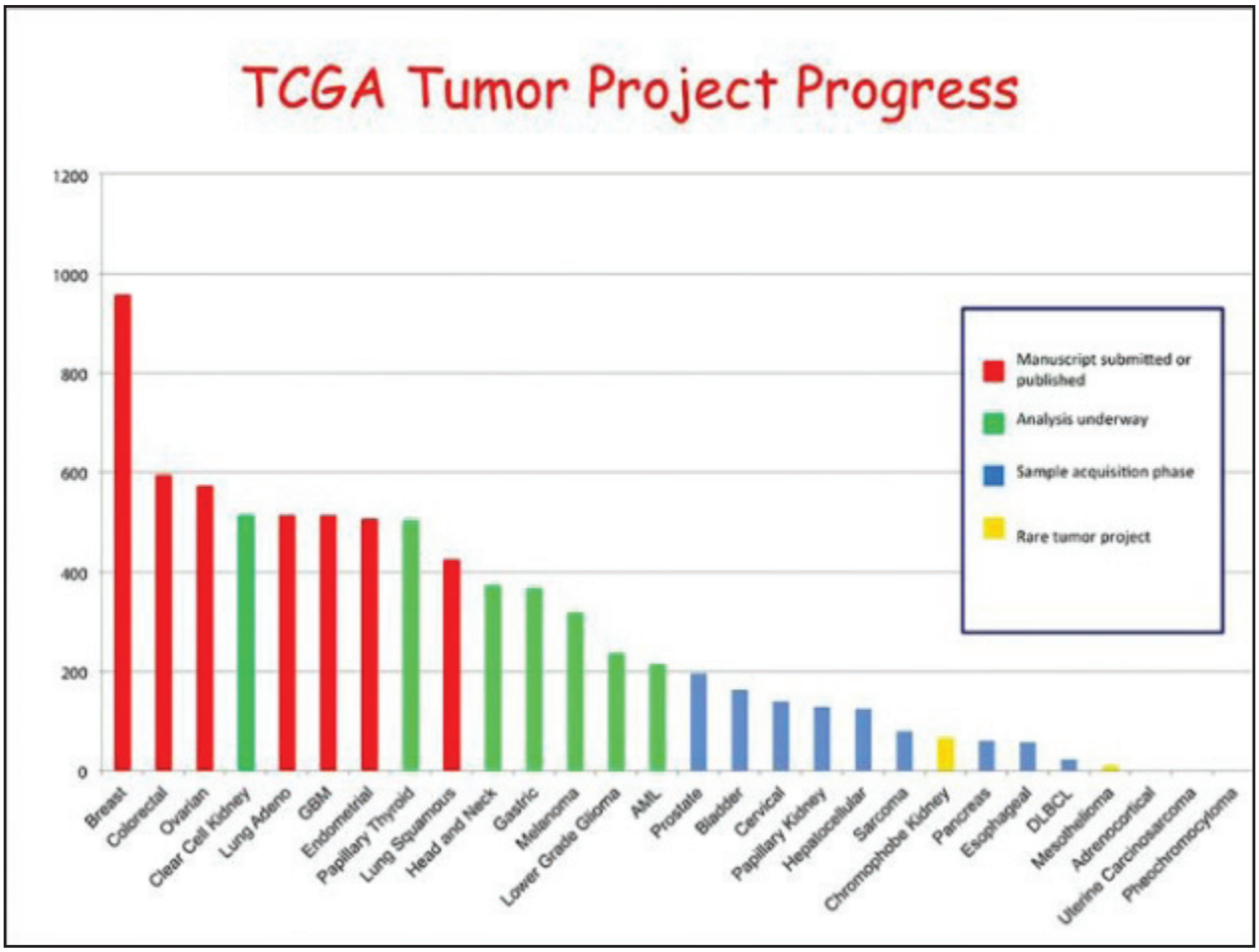
In many cases, these reports have already been published, in many cases, they are approaching publication, in some cases, we are still collecting samples.

This project is on track for being brought to conclusion in the latter part of 2014. After that, parts of the TCGA network will be sustained to carry out a number of initiatives that will be developed by our new Center for Cancer Genomics, and you will be hearing more about that in due course.

One important feature of our drive toward precision medicine, we plan to being this year and next, is a set of clinical trials that are based on scientific ideas and are directed toward moving the entire oncology community toward precision medicine.

I will mention just briefly three categories of such efforts: one, based on the idea of moving from a clinical phenotype to a genotype, looking at patients who've had exceptional responses to therapies within or outside of clinical trials and figuring out why they had exceptional responses.

Secondly, a trial called the "match trial," not yet publicized, which we will be analyzing genetic information from at least 1,000 patients or more to identify patients who have mutations that can be



matched with existing pharmacological agents or immunological agents.

And thirdly, we're trying to improve the use of some targeted agents that are already available. For example, crizotinib and erlotinib for certain forms of lung cancer, and the idea is to test those drugs as adjuvants in appropriate patients who've had lung cancer surgery for early stage lung cancer.

So, to give you a little more information about one class—the exceptional responders class—we know that a few percent of patients do respond in the context of clinical trials that don't receive FDA approval for that indication, and we're going to be using the methods that have been refined through TCGA to look for factors that might explain those exceptional responses.

And we believe this could lead to the development of predictive assays and improve our understanding of the origins of those cancers, and we're encouraged by a couple of examples of success.

Let me talk briefly about something I've spoken about here before, and many of you been hearing about since I became director almost about two and a half years ago, and that is the provocative questions initiative.

Now I'll remind you that in this time of fiscal drought we've been trying to focus the scientific community through a dialogue with the community on unanswered important questions that are difficult, but nevertheless present high risk and potentially high reward opportunities.

And the idea is these questions should build on specific advances that have been made. Secondly, address broad issues on the biology of cancer—be likely to lead to some progress and overcome obstacles in achieving some of our long-term goals.

Next, let me tell you a few things about how this works. We've been conducting workshops around the country and at NIH that have involved many thousands of scientists already to help to define these questions.

We've created a website for posting and reading and responding to the questions. We carried out an RFA last year that requested proposals to answer 24 of the provocative questions that have been agreed upon as high-priority ones. And we received an overwhelming number of applications—only able to afford to fund about 50 grants, but this year, we have made other

requests for proposals.

And this is for a partly overlapping set of questions—we've received a few hundred but not as many applications as last year, and we urge all of you, of course, to look at these questions and consider whether you have an interest in trying to answer some of them.

A couple of examples of such questions—we want in the long run to try to reduce of the overtreatment we're giving to many patients who are diagnosed with early stage cancers who never go on to have a lethal cancer by learning how to distinguish between those early lesions, the prostate, the breast, possibly even the pancreas, that currently are being very vigorously treated.

And tools for doing this, I believe, are available, but the answers are not yet clear.

Another important question is why some disseminated cancers can be cured by chemotherapy alone. And here is an iconic figure who obviously benefited from treatment with cisplatin, for treatment of metastatic cancer and has been cured.

A third initiative is one that has been going on at the Frederick National Laboratory for Cancer Research, previously known to many of you as the NCI at Frederick, and I want to review very briefly what's going on there as a way of emphasizing the importance of making use of this critical government-owned but contractor-operated facility.

This laboratory is on an old campus of Fort Detrick—the contractor there, SAIC, continues to provide important service to many of you in the extramural community, and some of us in the intramural community.

It has a new name, which sounds like the names of the important national labs in the Department of Energy and other departments. It has new leaders within SAIC, it has a new advisory group headed by Zach Hall, that has been guiding us and making this a more ambitious and more productive organization. And we have new leaders within SAIC including Dave Heimbrook, who's recently arrived from industry about a year and a half ago.

We have new facilities, which is the building shown in the bottom part of this slide that has yet to become occupied. And we have some new projects that emphasize the ambitions we have for the Frederick National Lab.

The first of those, is a project known as the RAS project, and the idea is to finally, after 30 years, learn how to target the cancer cells that exist in somewhere around a quarter of all human tumors that are driven by mutations in RAS and in other tumors where other mutations in adjacent genes affect the behavior of RAS.

That means taking advantage of new advances and structure of RAS proteins and affiliated proteins and new tricks in chemistry, understanding of signaling pathways, new possibilities in immunotherapies, the potential of synthetic lethalities to develop some new efforts.

Your current president, Frank McCormick, and I ran a workshop in San Francisco to lay out some of these possibilities, and Frank and I continue to work to try to develop these initiatives which will be conducted at the Frederick National Lab.

The second initiative involves enhancing the models we currently have for preclinical testing of drugs and other therapies, and that includes use of PDX libraries and other kinds of xenograft libraries and other means of studying tumors in mice to genetic engineering and so forth, better pharmacology tests, combination therapies and other things that are important in developing a synchronized effort that we are conducting with industry to improve the way we test therapies in a preclinical setting.

A fourth initiative I want to emphasize here is global health. We all recognize that the advances we made against cancer in the advanced economies need to be brought to bear in parts of the world where life expectancy is getting longer and the potential for preventing and treating cancer has yet to be adequately realized.

So we set up a center for global health a couple of years ago, run by Ted Trimble, and we have five general categories of ambition, and I'm going to review them very briefly. First is to assist development of registries and national cancer plans in many countries, and indeed we're already working with Mexico, Turkey, China, and many other places, and believing that you can't study it unless you can count it and we're making a lot of progress there.

Second, we taking advantage of the fact that infection-caused cancers are common in developing countries, 25 percent on average, 60 percent in some countries and we're trying to take advantage of especially some of the virus-induced cancers—particular focus on human papillomavirus-induced cancers, trying to get the vaccines that are available more widely used.

We're trying to take advantage of the fact that many risk factors for cancer, including tobacco obesity and alcohol are factors that place people at risk for

several other diseases, and we're working with our colleagues at other institutes that have a deep interest in global health to try and promote avoidance of those risk factors.

We are looking to improve the way in which healthcare and science operate in poor countries—helping them institute screening methods, adopt better means for using their health systems to provide access to treatment and symptom control, to perform surgery and do other things that are implicit in bringing better cancer control to poor countries.

And I'd like to mention, in a little more detail, the fifth point, that is to harness the enthusiasm that this society and many others—industry, professional groups—have had about advancing cancer control in poor countries and we're finding partners and building capacity in ways that I'm going to show in the next two slides.

The first example is the interaction we've had with many of our NCI-designated cancer centers that have been critical in developing cancer control in poor countries: in this case, the Fred Hutchinson Cancer Center which has developed a strong relationship with a long-standing cancer institute started initially by the NCI in Uganda in 1967, and recently ground was broken for a new center building that is funded by another U.S. agency (USAID), the government of Uganda and the Fred Hutchinson Cancer Center.

Another example provided in the next slide, which shows a figure and a brief piece of the summary from a recent commentary that the head of Cancer Research UK, Harpal Kumar, and I wrote in Science Translational Medicine recently talking about the various in which funders of medical research, and cancer research in particular, in many different countries, can work together to help place into practice some of the principles of cancer control, prevention, treatment, risk reduction and other things that we believe to be important, and I encourage you to have a look at this.

The Cultural Change

Finally, let me say a couple of words about cultural change.

We are living in tough times and it's important that the culture of cancer research, which all of you represent, operate in the best possible way. And let me mention just three general categories of change that I believe to be important.

First, sharing. You heard a very nice example from [Harvard Medical School assistant professor of medicine] Jay Bradner a few moments ago about the sharing of reagents, but also the sharing of results, the sharing of research reports through open access and public access to the scientific literature, reporting the outcomes of clinical trials as a particular interest to NCI and we will be initiating, during the coming year, some ways to further ensure that clinical trials, negative or positive, are adequately reported.

This is a critical element in a time when the public is looking to us to be sure that we're making optimal use of the funds that we have for doing cancer research.

Second, we need to acknowledge the claims that have been made now in several publications that some results from our investigators cannot be adequately replicated.

The NCI, along with many of the institutes at NIH, are paying special attention to this issue and the NCI has been providing standards to journals that publish articles that are funded by the NCI.

We are paying attention to other ways that we can try to provide encouragement and conviction on the part of the public that their money is being used to produce results that can be relied on.

I know this is a difficult and sensitive issue and we are going to move with delicacy, but this is an important issue for us to pay attention to.

The third point is one that concerns many of us who believed that the process of evaluation—a process which is increasingly important as money gets tight, when you are an applicant for a grant or an applicant for precision, that that process be fair and not solely depend on whether you publish in certain hyper-prestigious journals but instead, have done good work.

So the NCI will be doing a pilot experiment this year in which we use a revised bio sketch based on the kind of bio sketch that's been popularized at some academic institutions and Howard Hughes Medical Institute, in which you'll be asked to describe your five leading contributions to science as a way of helping a reviewer to evaluate your contributions rather than depending on where your named is positioned in a paper with 15 authors or 500 authors and instead focus on the contribution you have made to the scientific process.

We know that progress has been great and we believe, I believe, that while we have a complex and difficult opponent in the set of diseases that we are trying to encounter, we do have better tools, we have more information, we have yet greater talent, unfortunately we have less money, but we can do a lot, so let's do the best we can.

In Brief

ASCO Draft Recommendations Define Meaningful Trial Outcomes

(Continued from page 1)

expected from clinical trials in order to offer patients a meaningful benefit. The document focuses on pancreatic, lung, breast and colon cancers.

ASCO is inviting public comment on the document, which is posted through May 1 on ASCO's website.

The society hopes that participants, investigators and sponsors will have clearly defined expectations when considering clinical trials.

After the comments have been compiled and analyzed, the working groups for each disease and the full Cancer Research Committee will finalize the recommendations and send them to the board of directors for review. The guidelines would then be submitted to a journal.

Cancer Research Committee Chair Lee Ellis will participate in an educational session at the society's annual meeting to discuss the recommendations. Ellis is director of the Colorectal Cancer Translational Research Program and professor of surgery in the Department of Surgical Oncology at MD Anderson Cancer Center.

"Once we have reached consensus on the research outcomes that would be meaningful for patients, we hope to work with patient advocacy groups to encourage implementation of the outcomes by trial sponsors and investigators," Ellis said. "We would encourage trial sponsors and investigators to prioritize studies that use the consensus outcomes."

The society said that the Cancer Research Committee's effort to define clinically meaningful outcomes for clinical trials is consistent with the November 2011 publication of the ASCO report "Accelerating Progress Against Cancer: ASCO's Blueprint for Transforming Clinical and Translational Cancer Research."

BRIAN DRUKER, PETER NOWELL, and **JANET ROWLEY** were named the recipients of the **Albany Medical Center Prize** in Medicine and Biomedical Research for their contributions to the treatment of chronic myeloid leukemia.

The $500,000 award, one of the largest prizes in medicine and science in the U.S., will be awarded May 17. Five Albany Prize recipients have gone on to win the Nobel Prize.

Nowell is the Gaylord P. and Mary Louise Harnwell Professor Emeritus in the Department of Pathology and Laboratory Medicine at the University of Pennsylvania Perelman School of Medicine.

Nowell's research was the first to show that a genetic defect could be responsible for cancer. In 1960, as a faculty member at the University of Pennsylvania School of Medicine, he and graduate student David Hungerford of Fox Chase discovered a chromosome in blood cells from patients with chronic myeloid leukemia, which at the time was incurable.

This pivotal discovery was later named the Philadelphia chromosome.

Rowley is a professor of medicine and the Blum-Riese Distinguished Service Professor at the University of Chicago. Her discoveries of consistent chromosome abnormalities in leukemia secured a common agreement by the 1970s among scientists, physicians, and the general public that cancer is, in fact, a genetic disease.

In 1973, Rowley, a geneticist at the University of Chicago, was working on novel approaches to studying chromosomes, including Q-banding. Using this technique, Rowley discovered that Nowell's Philadelphia chromosome defect was the result of a translocation between chromosomes 9 and 22.

Druker is director of the Knight Cancer Institute and associate dean for oncology at Oregon Health & Science University. The earlier work of Nowell and Rowley paved the way for Druker to develop a treatment for CML that specifically targets the leukemia cells without harming healthy cells.

Once scientists understood the chromosomal nature of leukemia, they were able to determine that the malignant cells in CML contain the protein tyrosine kinase that caused an overproduction of white blood cells.

He and his colleagues identified the compound that ultimately became Gleevec (imatinib). Druker then led the drug's clinical trials. Nearly all CML patients saw their white blood counts return to normal in a matter of weeks with little or no side effects.