THE CANCER LETTER

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

Vol. 37 No. 23
June 10, 2011

Prepare for "Tsunami" of Genomic Information, Sledge Urges in ASCO Presidential Address

By Paul Goldberg

In his presidential address at the annual meeting of the American Society of Clinical Oncology, George Sledge attempted to describe the practical challenges of advances is genomics.

Speaking to clinicians June 5, Sledge, the Ballve-Lantero Professor of Oncology and professor of pathology and laboratory medicine at the Indiana University Simon Cancer Center, said that genome sequencing is becoming less expensive, and the day when a patient walks into her oncologist's office carrying a memory stick containing personal genomic data could be less than a decade away.

"When data are that cheap, every patient's cancer will be informative for tumor biology," Sledge said. "And things will get very, very complicated."

Sledge challenged his colleagues to think broadly, panoramically. The questions asked by oncologists both in clinical trials and in daily clinical practice would have to change, he said. The system of clinical trials, the writing of guidelines and the training of doctors will have to change, too.

"We need, both in our training and in our clinical practices, to redefine what it means to be an oncologist," Sledge said. "If oncology is the study of cancer biology, then the definition of the oncologist of the future must be a

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NCI News:

Doroshow Named Deputy Director, Clinical Research; Wold Takes One-Year Job at NCI Center for Genomics

JAMES DOROSHOW was named **NCI deputy director for clinical research**. Doroshow is the director of the Division of Cancer Treatment and Diagnosis.

The division will have joint managers: **Joseph Tomaszewski**, who serves as deputy director and **Jeffrey Abrams**, director of the Cancer Therapy Evaluation Program.

In other key appointments:

• **Barbara Wold** took a one-year job as director of the **Center for Cancer Genomics** while on leave from the California Institute of Technology.

• **Edward Trimble**, was named acting director for **the NCI Center for Global Health**. He remains in his job as head of gynecological cancer therapeutics at the Cancer Therapy Evaluation Program at NCI.

• **David Heimbrook** was named chief executive officer of **SAIC-Frederick Inc**. He joined the company from his job as head of discovery for the Oncology Discovery and Translation Area of Hoffman-LaRoche Inc.

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"Vibrant" Trials System a Must In New Era of Cancer Genomics

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clinical cancer biologist."

Even now, it's clear that complexity of cancers falls onto a spectrum. On one end are cancers Sledge describes as "stupid." They are driven by a single dominant mutation and have a small mutational load.

"Smart" cancers are on the other end. They have multiple drivers and carry many mutations. Multiple drivers have to be targeted to control them.

"The implications of these examples for individual patients with cancer are fairly obvious," Sledge said. "Genomic chaos forms the basis for the 'smart tumors' that cause so much harm. This is as much a quantitative as a qualitative problem. These tumors aren't hard targets, because we haven't found a single 'magic bullet.' There will be no 'magic bullet' for these tumors, because they don't have a single driving mutation: we need to think in terms of a 'magic shotgun,' loaded with pellets aimed at multiple targets in multiple pathways."

Sledge proposed a new concept for clinical trials of the future. To determine the sample size, clinical trialists would have to determine the "number needed to study." The math would be similar to calculation of the number needed to screen in a screening trial or number needed to treat.

"To predict how many patients we need to screen for every patient we study in a clinical trial, we would need to know the fraction of patients who are biomarker-positive for a particular kinase target, and therefore candidates for our targeted therapy," Sledge said. "Assays are never perfect, so we need to have a fudge factor taking this into account. Only a fraction of patients are trial-eligible, and not all of them will give their informed consent."

Sledge suggested a hypothetical case: attacking HER2 for the first time. Trialists would likely have to screen around 14 metastatic breast cancer patients to find one who would enter the clinical trial.

But the real-life situation will get more complicated.

"Now imagine we perform the same exercise with two kinases, one occurring in a quarter of metastatic patients and the other in 8 percent of patients," Sledge said. "Assume the diagnostic tests are 90 percent accurate, half of patients are trial-eligible, and 80 percent of those give their informed consent. If we are dealing with a two-drug combination the number needed to study is 154. Who in their right mind would screen 154 patients to enter one on a clinical trial?

"And forget three-drug combinations of novel agents.

"What happens when the next ten patients you see require eight different combinations based on their tumor genomes? Our current system is not designed to handle genomic chaos," he said. "It emphasizes single agent trials. It virtually never employs multiple biomarker-driven studies—and biomarkers will be required to validate the genomics. In most studies, biomarker development and analysis are of secondary importance at best.

"Finally, we have a regulatory apparatus that is ill-suited to the emerging biologic reality."

The excerpted text of Sledge's address follows:

The cost of healthcare outpaces inflation, and is the major cause of arguments over healthcare. But the cost of cancer care, and in particular the cost of cancer drugs, has soared in the past decade. And a recent analysis, published by Mariotto and colleagues in the JNCI, has suggested that by 2020, costs will increase another 27-39 percent. This is based solely on the changing demography of cancer in the U.S. and will occur even if no new drugs are approved. These trends are not sustainable.

Though doctors providing care are not responsible for the cost of these drugs, we are responsible for their appropriate use. We witness the effects of these costs on our patients, and we will be a target for many wishing to control health care costs.

What about new therapies? The clinical trials

THE CANCER LETTER

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

Subscription $395 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

workforce is dwindling in the United States. Overall, there has been an annual 3.5 percent decline in U.S.-based investigators since 2001—even as there has been an absolute and proportional increase in investigators based outside of the U.S. We welcome an international increase in clinical trialists, but a steady decline in the U.S. clinical trials workforce is real cause for concern. Clinical trialists are the bridge linking laboratory vision to patient care.

Being a clinical trialist is hard work; it is poorly compensated; it has been for some time a labor of love. Labors of love can be derailed by abusive relationships with unsupportive partners.

The challenges to participation in research trials are many, as outlined in a 2010 report issued by the Institute of Medicine. The pace of clinical cancer research is threatened even as scientific knowledge continues to explode. These are largely self-inflicted wounds, human in cause and therefore amenable to human solution, given sufficient resources and political will.

At the same time, the success rate for phase III trials in oncology remains abysmally low: we are just not good at picking winners compared to every other medical specialty. Why this is the case is undoubtedly complicated. I suspect that many of the failures have their roots in our incomplete understanding of tumor biology and the imperfect lessons we receive from early stage trials, where the signal to noise ratio is low.

None of these challenges are news to this audience. You live with them every day. But I would like to suggest to you that we face a new challenge, a challenge full of promise: this is the challenge of the genomic era.

In calling this the genomic era, I am well aware that genomics is accompanied by transcriptomics, proteomics, metabolomics, epiegnomics, pharmacogenomics and no doubt ten other "omics"; but let genomics stand as the surrogate marker for the tsunami of scientific knowledge bearing down on us.

Cancer therapy has gone through several different but overlapping eras. The oldest, beginning in the 19th century, was an era of local-regional therapy. Nonspecific systemic therapies came to the fore starting in the late 1940s and early 1950s, followed by targeted therapeutics. Targeted therapeutics exploded in the past decade, as the fruits of laboratory studies of cancer biology were translated to the clinic. We are now, I would suggest, just beginning to enter a fourth era, the era of genome-based therapy.

Most of these have only been attacked with therapeutic intent in the past decade. This is an ongoing revolution based on a simple yet powerful principle: find the driver of growth for a cancer in the laboratory; measure it in the clinic; then attack it with a specific targeted therapy—typically an antibody directed against a receptor or a small molecule hitting an internal kinase pocket.

Any rational person would hesitate to suggest that the era of targeted therapy—which is represented in our plenary session and in many oral presentations at this meeting—is over. We continue to find and treat novel targets, and treatments for several of these targets continue to evolve with the promise of increasing success. So why do I suggest that we are moving into a new era, a genomic era?

The first two human genomes were decoded in 2001, at the cost of over $3 billion. The first complete sequencing of human cancer genomes was published less than three years ago. As recently as this last year, the deep sequencing of a single patient's cancer was enough to get a paper published in the journal Nature. Today, as a result of efforts such as the NIH's Cancer Genome Atlas Project and the International Cancer Genome Consortium, several thousands of cancers covering 20 major tumor types are being sequenced.

Such large-scale sequencing will rapidly change our understanding of cancer biology; it will identify new targets in previously hard to treat diseases; and it will explain the causes of drug resistance. Within the next few years, perhaps by the end of this decade, we will likely see the beginning of population-based deep sequencing of patient's tumor genomes.

In addition to tumor genomics, genomic analyses of the host proceed apace. Genome-Wide Association Studies involving large swatches of the human genome are now becoming routine. Such studies will provide valuable insights into variations in drug response and toxicity. For instance, my colleague Bryan Schneider today will report the results of a GWAS study at a Clinical Science Symposium devoted to host genomics, implicating a previously unrecognized genetic source of variation in taxane-induced peripheral neuropathy.

Host genomics, combined with tumor genomics, will represent the basis for an individualized understanding of risk and benefit in the not-too-distant future.

Underlying these developments is the rapid fall in the price of whole genome sequencing. Indeed, the fall in the cost of sequencing is occurring at a more rapid rate than the regular fall in the cost of microprocessors, known as Moore's Law. We are on the verge of what specialists in the field refer to as the $1,000 genome, the cost point at which personalized genomics becomes

possible.

So what happens when, a few years from now, a patient walks into a doctor's office and hands a physician a memory stick loaded with gigabytes of personal genomic data?

Lest you think this prospect ridiculous, bear in mind that if you are willing to pay for it, you can already get your host whole genome sequenced and delivered to you on a USB drive, albeit at a still substantial price. Tumor genomes will not be far behind, though it will be several years before we have appropriate analytical tools available for everyday practice. But have no doubts, the genomic era is headed our way.

When data are that cheap, every patient's cancer will be informative for tumor biology. And things will get very, very complicated. We will actually be able to measure the degree and kind of mutations in an individual's tumor. This "in your face" genomic analysis will profoundly affect our understanding of etiology, prognosis and therapy for cancer patients.

The promise of this era is revealed by a recent paper in JAMA, in which deep sequencing of a patient's leukemic cells revealed a previously cryptic fusion oncogene amenable to therapy with a retinoic acid receptor inhibitor. This is the very first case, to my knowledge, of whole genome sequencing leading to individualized therapy in cancer, but it will certainly not be the last. We can look forward to a future in which the unraveling of the secrets of the genetic code is commonplace, expected, and routinely drives care. But this case, as wonderful as it is as a harbinger of our collective future, is not the whole story. Not every story will end this happily.

My sense of the past decade is that human cancers are segregating out based on the number of mutational drivers of growth, invasion, and metastasis.

Let's call them "stupid cancers" and "smart cancers," an oversimplification that serves to identify two ends of a spectrum.

"Stupid cancers" have a single dominant mutation and a small mutational load.

Targeting that dominant driver is regularly effective, and resistance is rare, often occurs late, and can frequently be reversed via other attacks on the same pathway.

Smart tumors have multiple simultaneous drivers, carry a large mutational load, and require the targeting of multiple drivers. Resistance is common in smart cancers and occurs early into treatment.

In the era of targeted therapy we have focused on specific mutational events: BCR/ABL, c-Kit, HER2, JAK, BRAF and others.

But the new currency of the genomic era, layered on top of our prized single driver mutations, is mutational load, measured in mutations per megabase.

I thank Gaddy Getz of the Broad Institute for allowing me to share this data with you.

Looking at greater than 1,000 whole exomes from various tumor types, we see that mutation rates can vary by more than 1,000 fold.

Several hematologic and childhood tumor types are at the low end with less than one mutation/Mb; head and neck cancers, colorectal cancer, lung adenocarcinoma and squamous cell cancers and finally melanoma have a median close to 10 mutations/Mb and can reach 100 mutations/Mb.

How does this play out in the clinic? The prototypical "stupid" cancer is CML. This once highly lethal disease is driven by a single chromosomal translocation. Targeting the product of that BCR-ABL translocation resulted in a high response rate and long survival times with imatinib, the very first drug to come along. And if that drug fails, just use another "ib" targeting the same kinase domain. I do not mean to denigrate either the groundbreaking research that led to imatinib or the use of these drugs: this is a true victory for targeted therapy and demonstrates its very real promise for cancer patients. But this is a stupid cancer.

In contrast, look at cigarette-induced non-small cell lung cancer. The first lung cancer genomes were published last year. To look at the Circos plot on the upper left gives you some sense of the challenge we face in this disease. In Circos plots, the chromosomes are arrayed in a circle. In the innermost ring, we see multiple inter- and intra-chromosomal rearrangements, either as long red lines crossing between chromosomes or short blue intrachromosomal loops. In the next ring, we see frequent loss of heterozygosity, followed by many copy number variations in the next ring and finally single nucleotide variants on the outside ring.

If we look now at the EGFR pathway from this patient, we see multiple points of amplification, loss of heterozygosity, and mutation—all within a single pathway. Because the investigators could count the number of mutations—and knew the patient's smoking history—they were able to determine that the patient's

tumor had one mutation for every three cigarettes smoked. This is a "smart" cancer.

It is no surprise that NSCLC has been resistant to so many different drugs. Indeed, it is surprising that any respond for any prolonged length of time. Similarly, it is no surprise that the targeted therapies such as EGFR and ALK inhibitors that work best in this disease work preferentially in nonsmokers, who carry a lower mutational load.

Remember last year's plenary session with the ALK inhibitor crizotinib? Three-quarters of ALK positive patients were never-smokers, and almost all of the rest ex-smokers. Do you want to respond well to a targeted therapy? The lesson seems to be that you need a single dominant driving mutation in a less-mutagenized cancer.

Or consider melanoma. At this meeting's plenary session we will see a genuine and exciting advance in melanoma therapy related to BRAF inhibition, another important victory in the era of targeted therapy. But BRAF inhibition, as this horrifying picture from a recent JCO publication suggests, will be hampered by the rapid emergence of resistance in some patients.

Indeed, even before the first presentation of the phase III trial of BRAF inhibition in melanoma, genomic analyses of tumors from patients undergoing BRAF-targeted therapy have revealed at least six separate forms of drug resistance.

Bear in mind that in the coming genomic era, such genomic chaos will be thrust in your face at a very early point. The challenge will to be to use our new knowledge to defeat a smart and treacherous foe.

And, of course, the genomic era is telling us what we already suspected: these tumors evolve, as this study of the primary and metastatic tumors of a pancreatic cancer patient suggest.

As the Circos plot in the upper left shows, some genetic lesions are seen in all metastases, some are partially shared, and some are private to the index metastasis, in this case the crucial KRAS amplicon on chromosome 12. In the upper right, looking at a panel of metastases from one patient, one can see that out-of-frame deletions of different types are found in different clusters of metastases.

This leads to a model of an evolving tumor, even before therapy is administered, in which a primary tumor gives rise to metastases that in turn give rise to genetically different secondary metastases. Genomic instability can defeat our best efforts in smart tumors.

The implications of genomic chaos go far beyond its impact on individual patients. Let's look at what happens in a clinical trial. Matt Ellis and his ACOSOG colleagues presented a wonderful study at the recent AACR meetings.

Fifty breast cancer patients receiving preoperative hormonal therapy underwent baseline biopsies for Ki67 testing and deep genomic sequencing. Ki67, a marker of proliferation, identifies patients as responders or non-responders, based on prior trial results in the preoperative setting.

Ki67 cuts this population into two equally sized groups. The first thing to notice is that responding tumors harbor, on average, half as many coding mutations as non-responders. Again, this suggests that in the genomic era smart cancers are smart at least in part for quantitative reasons: mutational load rules in the clinic.

But the real surprise is the sheer number of significantly mutated genes—and how many of these mutations occur at frequencies less than 5 percent. Once we get past some of the high-flying usual suspects, like PI3Kinase and p53, everything becomes a rare mutation, and suddenly we are dealing with a whole series of orphan diseases.

And that is only the beginning. Evolutionary biologists have a phrase, the "Red Queen Principle," derived from Lewis Carroll's Through the Looking-Glass, to describe the arms race between co-evolving species. Think of targeted therapies and smart tumors as being part of an evolutionary arms race. When dealing with smart tumors—where genomic instability constantly increases mutational load—are we doomed, like the Red Queen, to run faster and faster just to stay in the same place?

Well, perhaps, if we treat these targets one at a time. But as Jayne Stommel of the NCI has shown in the setting of glioma, while most smart tumors have multiple kinases activated, we can optimize cell kill by inhibiting all of them at the same time.

The implications of these examples for individual patients with cancer are fairly obvious. Genomic chaos forms the basis for the "smart tumors" that cause so much harm. This is as much a quantitative as a qualitative problem. These tumors aren't hard targets because we haven't found a single "magic bullet." There will be no "magic bullet" for these tumors, because they don't have a single driving mutation: we need to think in terms of a "magic shotgun," loaded with pellets aimed at multiple targets in multiple pathways.

So, let's assume—because it is probably true more often than we would wish—that cancers have multiple drivers, and that to cure a cancer—and let us use the word cure, for our patients deserve no less—that targeting them simultaneously increases benefit. So now imagine cancers with two drivers, requiring two different

kinase inhibitors. What is the number of patients we need to study the combination of two new kinase inhibitors?

I'd like to introduce a new concept, which I call "number needed to study," something different than number needed to screen or number needed to treat, though the math is similar.

To predict how many patients we need to screen for every patient we study in a clinical trial, we would need to know the fraction of patients who are biomarker-positive for a particular kinase target, and therefore candidates for our targeted therapy. Assays are never perfect, so we need to have a fudge factor taking this into account. Only a fraction of patients are trial-eligible, and not all of them will give their informed consent.

Imagine you are attacking HER2 for the first time. I've made these numbers up, so feel free to criticize, but you probably had to screen around 14 metastatic breast cancer patients for each one who eventually entered the clinical trial. It might be worse—I left out some other fudge factors.

Now imagine we perform the same exercise with two kinases, one occurring in a quarter of metastatic patients and the other in 8 percent of patients. Assume the diagnostic tests are 90 percent accurate, half of patients are trial-eligible, and 80 percent of those give their informed consent. If we are dealing with a two-drug combination the number needed to study is 154. Who in their right mind would screen 154 patients to enter one on a clinical trial? And forget three-drug combinations of novel agents.

There are, of course, some workarounds for this problem, developing less specific agents, fewer exclusion criteria, and smarter informed consents. But the basic problem remains: having multiple targets in small patient fractions means that drug development will be tougher in the genomic era.

Are there other approaches than the targeting of kinase networks, which as I have suggested may face daunting challenges? Of course. To name just a few:

We can increase our efforts at cancer prevention; you will recall that the most heavily mutagenized cancers—melanoma and lung cancer—represent self-inflicted wounds.

We can harness the body's immune system; our plenary session includes one such example.

We can attack tumor stem cells.

We can redouble our efforts to interfere with DNA damage repair mechanisms.

We can interfere with the tumor microenvironment.

And we can invoke metastasis suppressor gene products.

What happens to clinical trials in the era of genome-driven therapy? For those interested in developing agents targeting specific pathways or networks, the task is a daunting one for smart cancers. We will be faced with large numbers needed to study, as I have suggested.

What happens when the next ten patients you see require eight different combinations based on their tumor genomes? Our current system is not designed to handle genomic chaos. It emphasizes single agent trials. It virtually never employs multiple biomarker-driven studies—and biomarkers will be required to validate the genomics. In most studies, biomarker development and analysis are of secondary importance at best. Finally, we have a regulatory apparatus that is ill-suited to the emerging biologic reality.

How will we meet the challenges of the genomic era as a profession? Will we be passive recipients of, or active participants in, this scientific revolution? I would suggest that we must work to meet the challenges of this new genomic era. We need a trained and motivated workforce. We need a vibrant clinical trials system. And we need to pioneer a rapid learning system for oncology.

Let me touch on each of these points briefly.

I have already mentioned the challenges facing this workforce, challenges each of you is aware of. We will need a workforce that understands the principles underlying the genomic revolution—and an environment that supports the difficult work we do. And we need adequate numbers to face the rising volume of cancer patients and new agents headed our way.

In particular, we need, both in our training and in our clinical practices, to redefine what it means to be an oncologist. If oncology is the study of cancer biology, then the definition of the oncologist of the future must be a clinical cancer biologist.

We will need a vibrant clinical trials system.

ASCO supports the full implementation of the recent IOM report's recommendations on the Cooperative Groups, with increased efficiencies resulting from functional reorganization of the federal clinical trials system—as well as the resources appropriate to the tasks required by those trials.

The genomic revolution will place special emphasis on the incorporation of translational science endpoints, increasingly derived from whole genome sequencing of individual patient's tumors, in every trial.

This is currently just a dream, but the falling price of genomics should make this a reality in the not-too-distant future, and it is not too early be planning the first generation of whole-genome-based trials, as Matt Ellis and his ACOSOG colleagues have shown us. Some in this audience may wonder if the cooperative groups have

a future in the genomic era. I would suggest to you that the genomic era will require the reinvigoration of the cooperative groups to succeed.

We have Next-Gen sequencing. We need a "Next-Gen" clinical trials system, based on personal genomics, with real-time bioinformatics. The Number Needed to Study problem suggests a need for extensive health information technology systems linking clinical researchers, drug developers, tissue banks and laboratory scientists—and linking them worldwide.

If we are to attack multiple targets simultaneously, we need investigators at many centers testing multiple combinations, those combinations to be derived from genomic analysis of the primary or metastatic tumors of individual patients. Underlying this is a need for greater collaboration, particularly among companies developing new agents. We need new clinical trials designs that allow the simultaneous study of multiple combinations. This will also require redesign of the informed consent process and of our regulatory apparatus.

None of this is easy, but all of it is necessary.

What will be the role of our professional society in this new era? If the health system for oncology is to succeed, all its parts must be healthy and connected. We can begin to make this a reality by committing to a concept called the Rapid Learning System. Described by Lynn Etheredge and advanced by the Institute of Medicine, a rapid learning health system leverages information technology to bring real time innovation to both science and practice. By bringing our communities closer—by linking research to practice—by connecting through technology as well as patient-focused human interaction—we can achieve an international system that will bring us to greater insight to this disease and better care for our patients.

As an organization we view this Rapid Learning System as having three important elements: Health information technology, guidelines, and performance measurement.

Health information technology will be central to the Rapid Learning System in the genomic era. Doctors will need real-time access to clinical data from all practice settings. This in turn will require interoperable databases using common terminology.

Health information technology should offer on-the-spot decision support to oncologists and patients facing the increasingly complex tapestry revealed by modern genomics. It should provide individualized, ready access to a clinical trials systems. It should support appropriate coverage and reimbursement for services. And it should aggregate data so that we can learn from every patient's experience.

There are real challenges facing us here, challenges involving cost, patient privacy, data ownership, and the dysfunctional silo mentality of health care systems across the globe.

ASCO is not an electronic health records company, but we do believe we have an important organizing role to play in creating the HIT systems of the genomic era.

Our approach to guidelines will also need to change in the genomic era. Guidelines will need to retain their intellectual rigor, but at the same time be flexible enough to deal with the hundreds—or thousands—of orphan diseases revealed by modern biology. They will need to be easily accessible, user-friendly, and add value to daily patient care. Clinical guidance across the full spectrum of cancer prevention, treatment and survivorship should, of course, form the basis for intelligent decision support for doctors and patients. The melanoma treatment finder launched by ASCO and CollabRx this year is a good example.

These are challenges that no current guidelines group has yet addressed. ASCO and its volunteers are the right agents of change for guidelines in the genomic era, but we are also happy to work with other guideline organizations on this challenging task.

The Rapid Learning System for Oncology will also require the development of quality measures. We need measures that are attached to a practice's electronic health records, seamlessly extracting information. These measures should be shared with patients, providers and researchers. They should be endorsed, when applicable, by national standard setting organizations. Their use should support physician accreditation and decision making and be part of an iterative feedback process.

ASCO's QOPI guidelines are a first step in this direction, but only a first step: much work remains.

ASCO is the right organization to take on this task. Physicians should judge physicians using a meaningful and agreed upon set of patient-focused quality measures. Creating a unified set of measures and standards for our profession is far superior to having a legion of measures imposed on us by a multitude of dueling sources, something that is increasingly—and alarmingly—the case.

As we go forward in the genomic era, we must be willing to look back. Back to the humane standards that have forever guided our profession. Back to our belief that patients always come first. Back to the realization that the pathways forward all flow from that which is best in the human spirit: our thirst for useful knowledge, our compassion for our fellow beings, and our belief in their essential dignity.

NCI News:

Abrams, Tomaszewski Named To "Jointly Manage" DCTD

(Continued from page 1)

NCI Director Harold Varmus announced the appointments in a memo dated June 2.

The text of the document follows:

As you know, I have been working for the past few months to fill number of key positions here at NCI. I am pleased to tell you about some of them today.

First, I am delighted to welcome Jim Doroshow to his new role as NCI Deputy Director for Clinical and Translational Research. Jim has been the Director of the Division of Cancer Treatment and Diagnosis (DCTD) since 2004, and brings tremendous institutional and scientific knowledge about clinical investigation to his new position.

DCTD, meanwhile, will be jointly managed by current DCTD Deputy Director Joe Tomaszewski and DCTD Cancer Therapy Evaluation Program Director Jeff Abrams.

I am also pleased to announce that Barbara Wold will be joining NCI as Director of the Center for Cancer Genomics for a year while she is on leave from her position as Bren Professor of molecular biology and Director of the Beckman Institute at Caltech. She has been a member of the Caltech faculty since 1981; she brings rich experience and insight to the Center from her work developing innovative new tools in bioinformatics such as RNA-Seq and her discoveries in molecular genetics, genomics and regulation of cell fate. She will begin her new assignment Sept. 1.

Ted Trimble, who currently is Head, Gynecological Cancer Therapeutics in the Cancer Therapy Evaluation Program at NCI, has also begun to serve as Acting Director for the new NCI Center for Global Health. Ted worked to set up the trans-NCI International Clinical Trials Collaboration Working Group in addition to other global health experience that will be helpful in launching the new Center.

And lastly, as I noted in an earlier announcement, Science Applications International Corporation (SAIC) has selected David Heimbrook as chief executive officer of SAIC-Frederick, Inc. David, who joined SAIC from his current post as the global head of discovery for the Oncology Discovery and Translation Area of Hoffman-LaRoche, Inc., began his new duties May 31.

Please join me in welcoming these folks to their new positions.

— Harold

ASCO News:

Anderson Gets Karnofsky Award, Weinberg Gets Science Prize

ASCO honored several individuals at its Annual Meeting in Chicago, June 3-7, for their contributions to the practice of oncology and their commitment to patients with cancer.

The award recipients include:

• **KENNETH ANDERSON, David A. Karnofsky Memorial Award and Lecture:** Anderson is the Kraft Family Professor of Medicine in the Department of Medicine at Harvard Medical School; medical director of the Kraft Family Blood Center at the Dana-Farber Cancer Institute; and an oncology physician at Brigham And Women's Hospital. He was recognized for his studies on novel biologically based therapies for multiple myeloma.

• **ROBERT WEINBERG, Science of Oncology Award and Lecture:** A founding member of the MIT Whitehead Institute, Weinberg is best known for his discovery of the ras oncogene and for the isolation of the first known tumor suppressor gene, Rb.

• **JAMIE VON ROENN, ASCO-American Cancer Society Award and Lecture:** Von Roenn, professor of medicine at the Feinberg School of Medicine at Northwestern University, has focused on the integration of palliative medicine skills and principles into oncology care.

• **LUCA GIANNI, Gianni Bonadonna Breast Cancer Award and Lecture:** The director of medical oncology and coordinator of the New Treatments' Development Programme at the Istituto Nazionale Tumori, Milano, Gianni's research has led to the definition of a successful new regimen for breast cancer, and has clarified relevant aspects of the pharmacology of paclitaxel, as well as the mechanisms of drug–drug enhancement with doxorubicin.

• **JOHN BENNETT, B.J. Kennedy Award and Lecture for Scientific Excellence in Geriatric Oncology:** Bennett, Professor Emeritus of Medicine at the James P. Wilmot Cancer Center at the University of Rochester Medical Center, was a founding member of the International Society for Geriatric Oncology and the first chair of the Myelodysplastic Syndromes Foundation.

• **LEE HELMAN, Pediatric Oncology Award and Lecture:** Helman, head of the Molecular Oncology Section and a senior investigator at NCI, has focused his research on the biology and treatment of pediatric sarcomas, specifically Ewing's sarcoma,

rhabdomyosarcoma, and osteosarcoma.

• BENJAMIN ANDERSON, Partners in Progress Award: For the past decade, Anderson, professor of surgery and global health medicine at University of Washington, has worked in the international breast cancer clinical improvement and best practices movement through the establishment of the Breast Health Global Initiative.

• DAVID KHAYAT, Distinguished Achievement Award: Khayat, president of the French National Cancer Institute, organized the French Federation of Medical Oncologists, and was the co-founder of the World Summit Against Cancer, which gathered more than 100 international leaders to reaffirm their commitment to the eradication of cancer.

• DANIEL HALLER, Special Recognition Award: Haller, the Deenie Greitzer Gastrointestinal Medical Oncology Professor at the University of Pennsylvania, was honored for his contributions to clinical oncology and cancer research, and for his dedicated service to the oncology community. He is the editor-in-chief of the Journal of Clinical Oncology, the official journal of ASCO.

• Sen. SHERROD BROWN (D-Ohio), Public Service Award: Brown ensured that the Patient Protection and Affordable Care Act included important consumer protections, requiring that insurance plans cover routine patient care for patients undergoing cancer clinical trials.

ASCO Statesman Award

The ASCO Statesman Award recognizes members for extraordinary volunteer service, dedication, and commitment to ASCO. Recipients have given 20 years of volunteer service.

The awardees include:

Dean Bajorin, Memorial Sloan-Kettering Cancer Center; **Julie Brahmer,** Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins; **Otis Brawley,** American Cancer Society; **Richard Goldberg,** University of North Carolina; **Lori Goldstein,** Fox Chase Cancer Center; **Daniel Haller**, Abramson Cancer Center, University of Pennsylvania; **Daniel Hayes,** Maine Center for Cancer Medicine; **Lee Helman,** NIH/NCI Center for Cancer Research; **Waun Ki Hong,** University of Texas MD Anderson Cancer Center; **Maurie Markman,** Cancer Treatment Center of America, Eastern Regional Medical Center; **Richard McGee,** Puget Sound Cancer Centers; **Robert Miller,** Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins; **Michael Neuss,** Oncology Hematology Care, Inc.; **Lisa Newman**, University of Michigan; **J. Chris Nunnink,** Vermont Center for Cancer Medicine; **Martine Piccart-Gebhart,** Jules Bordet Institute; **Kathleen Pritchard,** Sunnybrook Odette Cancer Centre; **Lidia Schapira,** Massachusetts General Hospital; **Joel Tepper,** University of North Carolina; and **Christopher Willett,** Duke University Medical Center.

In the Cancer Centers:

Weiss Named Chief Medical Officer Of Cancer Research Consortium

GLEN WEISS will head the Cancer Research and Biostatistics-Clinical Trials Consortium as its chief medical officer. The consortium represents more than 10 institutes worldwide, dedicated to funding and facilitating clinical trials.

"Our consortium's explicit mission is to organize and accelerate the clinical development of new agents for the treatment of patients with lung cancer," said Weiss, co-head of the Lung Cancer Unit and assistant professor at the Translational Genomics Research Institute and director of thoracic oncology at Virginia G. Piper Cancer Center.

CRAB-CTC members include laboratory and clinical researchers in the U.S., Canada and China.

FDA News:

Burris and O'Shaughnessy To Address Avastin Hearing

The Genentech list of witnesses for the June 28-29 hearing on the drug Avastin (bevacizumab) includes two individuals from outside the company: **Joyce O'Shaughnessy**, of US Oncology and Baylor Charles A. Sammons Cancer Center, and **Howard Burris**, of Sarah Cannon Research Institute.

Both will address "clinical perspectives on the treatment of HER-2 negative MBC."

The rest of the issues will be handled by Genentech staff. **Hal Barron**, executive vice president, global product development and chief medial officer, will present an overview of Genentech's position.

Sandra Horning, senior vice president and global head of clinical development in hematology/oncology, will present the clinical data and the company's proposed confirmatory study.

Biostatistical issues will be presented by **James Reimann**, global head of oncology biostatistics.

Michael Labson, an attorney with the firm of Covington & Burling, will present regulatory and legal

issues.

FDA's list of witnesses does not include any outside experts.

FDA's witnesses are: **Richard Pazdur**, director, Office of Oncology Drug Products; **Patricia Keegan**, director, Division of Biologic Oncology Products; **Lee Pai-Scherf**, medical officer/medical reviewer, Division of Biologic Oncology Products; **John Jenkins**, director, Office of New Drugs; **Abby Brandel**, associate chief counsel, Office of Chief Counsel.

Ultimately, political considerations could play a role in the decision (The Cancer Letter, May 27).

FDA Orders Providers to Cease Calling Thermography Superior

FDA officials warned women not to substitute breast thermography for mammography to screen for breast cancer.

Some health care providers claim thermography is superior to mammography as a screening method for breast cancer, because it does not require radiation exposure or breast compression.

To date, FDA has not approved a thermographic device for use as a stand-alone method for screening breast cancer. FDA has cleared thermography devices for use only as an additional diagnostic tool.

"Mammography is still the most effective screening method for detecting breast cancer in its early, most treatable stages," said Helen Barr, director of the Division of Mammography Quality and Radiation Programs at FDA's Center for Devices and Radiological Health. "Women should not rely solely on thermography for the screening or diagnosis of breast cancer."

FDA has issued warning letters to some health care providers who have been promoting the use of breast thermography. The letters instructed the providers to cease making claims that thermography devices, when used alone, are an effective means of detecting breast cancer.

"While there is plenty of evidence that mammography is effective in breast cancer detection, there is simply no evidence that thermography can take its place," said Barr.

Oncology Treatments Could Become One of Top Three Expensive Therapies

A drug trend report from Medco Health Solutions Inc. said that new cancer therapies, treating increasing numbers of patients, could drive up cancer drug spending by as much as 30 percent over the next two years.

At this rate, oncology drugs would likely rise to the second or third largest trend-driving category by 2015, behind diabetes and central nervous system treatments, according to the report which tracks utilization and spending.

Due to advances in treatment, the number of U.S. cancer survivors is expected to increase from 13.8 million in 2010, to 18 million by 2020.

This has increased the demand for oncology specialty drugs.

Targeted therapies have increased 6.7 percent according to the report. The drug trend for specialty cancer treatments reached 21.2 percent, due primarily to unit cost increases of 13.7 percent.

"Early diagnosis, evidence-based treatment and enhanced coordinated care have essentially turned some forms of the condition into chronic illnesses that can be managed longer-term," said Glen Stettin, Medco's chief medical officer. "Continued innovation, including companion diagnostic or pharmacogenomic testing, can help ensure the right person is getting the right drug at the proper dose and reduce waste."

Since many new specialty drugs have reached the market in recent years, oncology drug price inflation surged to 11.5 percent during 2010.

More frequent perscription of newer treatments—such as Revlimid, for multiple myeloma, and Gleevec, a tablet for chronic myeloid leukemia and gastrointestinal stromal tumors—has driven sharp increases in the trend, said the report.

More than 90 percent of anti-cancer drugs approved since 2004 cost more than $20,000 for a 12-week course of therapy, according to JNCI.

Higher generic drug dispensing helped limit prescription drug spending growth to 3.7 percent during 2010, the report said. Generics accounted for more than 71 percent of the prescription drugs dispensed. Generic drugs had a limited inflation rate of 0.5 percent and helped control overall prescription drug costs.

Specialty drugs accounted for 70.1 percent of overall drug trend. Both utilization and unit costs increased for these medicines, which treat rheumatoid arthritis, multiple sclerosis, cancer, and an array of other conditions.