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New NCI Director Proposes $9 Million "Community Cancer Centers Program"

By Kirsten Boyd Goldberg

In one of his first actions as NCI director, oncology surgeon and former cancer center director John Niederhuber proposed a $9-million, three-year pilot project that would aim to conduct research designed to help community hospitals coordinate state-of-the-art cancer care.

"We want to bring the science to the patients where they live," Niederhuber said to the National Cancer Advisory Board Sept. 6.

President Bush appointed Niederhuber as NCI director on Aug. 15 (see story, page 3).

The project, called the NCI Community Cancer Centers Program, would be funded as a subcontract through the institute's contract with SAIC and would support research at about six competitively selected community hospitals. The main requirements for the hospitals include a base of 1,000

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ODAC Nixes Abraxane In Adjuvant Breast Cancer, Genasense Falls Victim To Its Randomized Trial

By Paul Goldberg

American BioScience Inc. wanted to skip a few steps in developing its paclitaxel-based drug Abraxane.

Earlier this week, the company faced the FDA Oncologic Drugs Advisory Committee with a proposal to quickly move the drug approved for metastatic breast cancer all the way up to adjuvant treatment of node-positive breast cancer.

Arguing that Abraxane is just another form of Taxol, ABI wanted to skip conducting the large clinical trials the agency requires for approval of adjuvant therapies.

"Based upon the data, there is no scientific basis to hypothesize that Abraxane will be less effective as adjuvant therapy since Abraxane safely delivers a higher dose of paclitaxel than already proven to be effective in adjuvant setting and is proven to be superior in metastatic breast cancer," Clifford Hudis, chief of the Breast Cancer Medicine Service at Memorial Sloan-Kettering Cancer Center, said to the committee.

ODAC voted 13-1 against this proposal, upholding the agency's view that Abraxane, an albumin-bound formulation of paclitaxel, differs substantially from ordinary paclitaxel. Abraxane has a distinct safety and efficacy profile, different pharmacokinetics, and is administered in a different dosage and delivery schedule.

In a separate recommendation at the Sept. 6-7 session, ODAC shot

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NCI Seeks Comment On RFI For Community Cancer Centers

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new cancer cases a year and enrollment of 25 patients a year on NCI-supported clinical trials.

The research from the three-year pilot project—identifying health disparities and other factors that lead to less-than-optimal care—would be incorporated into a Request for Applications "that would establish this eventually as a permanent program within the NCI," Niederhuber said.

Niederhuber told the NCAB that he has been developing the project for the past year, since he arrived at NCI last September as deputy director for clinical and translational science. The program was presented to Congressional appropriators earlier this year, months before it was made public.

The House Labor-HHS-Appropriations Subcommittee's report on NCI funding for fiscal 2007 commended the institute "for its foresight in developing the community cancer centers program, which is a direct mechanism to translate the most promising advances in cancer treatment… to community hospitals around the country" (The Cancer Letter, June 30, 2006).

NCI released a Request for Information on Aug. 20, describing the proposed new program and seeking public comment. The text of the RFI is available at http://web.ncifcrf.gov/bizopps/rfps/RFIS06-285.doc. The deadline for submitting comments is Sept. 15.

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According to the RFI, the new NCCCP "will explore methods and structures to bring state-of-the-art oncology care and early phase translational science to the community hospital-based cancer center setting, utilizing linkages with other NCI sponsored research programs such as the Community Clinical Oncology Program, the Community Networks Program, and NCI-designated Cancer Centers, as well as with local, state and federal agencies and private sector-sponsored research activities. It will do so with the clear-cut goals of expanding access to cancer prevention, screening, treatment, survivorship follow-up and end-of-life care as well as increasing participation in early phase clinical trials, and reducing healthcare disparities."

Niederhuber said an internal NCI working group developed the proposal, and he had discussed it with several cancer center directors.

Christian Downs, executive director of the Association of Community Cancer Centers, said his organization would welcome the chance to talk with Niederhuber about the program. ACCC, begun in 1972, has a membership of about 750 hospital-based cancer programs and 250 physician group practices.

"We've got questions, our members have questions, and we'd love to be able to help our membership answer those," Downs said to The Cancer Letter. "I would hope NCI would work a little closer with groups like ours to make sure this program is a success. I don't feel we have been brought into the process as to what this is. We are an organization that would help make it a success, and I hope they reach out to us."

It is unclear how the proposed program would coexist with the NCI's chronically underfunded Community Clinical Oncology Program. Earlier this year, NCI officials told the CCOP principal investigators to slow accrual of patients to clinical trials due to budgetary concerns.

The 50 CCOPs and 13-Minority-based CCOPs in 35 states were on track to enroll nearly 8,000 patients on NCI trials from June 2005 to May 2006. From 2001 to 2003, CCOPs alone enrolled 7,000 to 8,000 people on large NCI prevention trials (The Cancer Letter, May 12, 2006).

CCOP, begun in 1983, allows investigators to enroll patients on most cooperative group trials, including phase I, II, and III trials, but the program appears to have had the most success in accruing patients to large prevention studies and phase III treatment trials.

"The CCOPs program is really for phase III trials," Niederhuber said to The Cancer Letter in an interview after his NCAB presentation. "This is really not about

expanding trials, it's really about changing practice and delivery, all the way from prevention and screening to the earliest phases of clinical trials, bringing science to where people live, bringing access to new molecularly-targeted agents and molecular characterization of tumors."

Asked by this reporter whether the project would attempt to create smaller versions of cancer centers, Niederhuber said, "You might think of it that way. They are not going to have the major research of the universities, but there is a whole other huge population of people who need care. This is to think about how can we elevate that boat, bringing science like highly characterized tumors to these patients."

"Fragmented" Cancer Care

Cancer care in the U.S. is "quite fragmented," Niederhuber said to the NCAB. While NCI's Cancer Centers Program is the "a star in the crown of NCI," many areas don't have easy access to a center. About 16 percent of cancer patients are treated at the 61 NCI-designated centers, he said.

"We have absolutely no way at present of delivering the science that we have today, and the science that we anticipate in the next several years, to the people at the community level," Niederhuber said. "I think that in many ways, the issue of access to state of the art care will be a greater determinant of mortality than any of the risk factors that we can think of, including tobacco."

Niederhuber, former director of the University of Wisconsin Comprehensive Cancer Center, said he and other center directors have tried networking with small hospitals and community practices to "build another rim of in the wheel of care extending out from the cancer centers."

The proposed new program would encourage those linkages and help reduce the fragmentation in cancer care, he said. However, the NCI funding would support research, not health care delivery, he said. "Remember, we are not about delivering health care," he said. "That's not our mission. Our mission is about research. We need to do research that tells us how to do better delivery of health care, how to do better translation, how to reach out to people in terms of education. So the program is a research program, not a delivery program."

The program also would encourage tissue banking, bioinformatics, and the development of electronic medical records, he said.

Eventually, NCI could offer the program as a resource for industry-funded trials, in effect acting as a contract research organization, he said.

"[A company] could meet with us with this entity… and in a matter of hours of signing the agreements, rather than months, we could work out those opportunities for clinical research," Niederhuber said. "We would be able to immediately open that up across the cohort of facilities across the country and accomplish something in a matter of weeks or months that might take us years to accomplish."

The small hospitals would be linked to one or more cancer centers, Niederhuber said. "I see it as a way of strengthening the Cancer Centers Program," he said. "It's a way for the centers to take translational opportunities to a much larger population and get trials accomplished in a shorter period of time."

Funding for the pilot project would come through subcontracts with SAIC, contractor for the NCI-Frederick cancer research center. Information technology, biospecimens, and clinical trials would each receive about 20 percent each, and the remaining

President Appoints John Niederhuber 13th NCI Director

By Kirsten Boyd Goldberg

President George W. Bush named surgeon John Niederhuber the 13th NCI director on Aug. 15.

Niederhuber joined NCI last fall as deputy director for clinical and translational sciences, but found himself suddenly elevated to a new post as the institute's "chief operating officer" when NCI Director Andrew von Eschenbach was named acting FDA commissioner. After von Eschenbach stepped down as NCI director earlier this year, Niederhuber was named acting NCI director.

Prior to joining NCI, Niederhuber was a professor of surgery and oncology at University of Wisconsin. He had been director of the university's Comprehensive Cancer Center from 1997 to 2002. He was asked to step down after medical school officials expressed disappointment in his fundraising efforts, according to news reports.

Niederhuber came to Wisconsin from Stanford University, where he had been chairman of the Department of Surgery. His demotion from that position in 1995 has been described as a result of intense academic politics (The Cancer Letter, Oct. 7, 2005).

Niederhuber served as chairman of the National Cancer Advisory Board from 2002 to 2005.

40 percent of the funds would support research in healthcare disparities.

NCI anticipates releasing a Request for Proposals in mid-October, with responses due in mid-December. Sites would be selected in mid-March and the program would begin on April 30.

NCAB Reaction: "Ambitious, Challenging"

Board members called the proposed project "ambitious" and "challenging."

"We had the health disparities PRG report done, but nothing happened," said Diana Lopez, professor of microbiology and immunology, University of Miami. "Could that be used as a guideline for this?"

"We have good programs in disparities," said Niederhuber. "What we've never been able to do is to put this all together in one site. One of the light bulbs went off in my head as we were sitting around the table was, gee, this is a laboratory. It's a community facility or a rural site, but it gives us a chance as NCI to bring a lot of our different programs to one site to see if doing these things in an integration fashion gives us a bigger bang than if we are doing this in isolation."

LYDIA RYAN, of Children's Healthcare of Atlanta: "It's a comprehensive, but ambitious program scorecard if you will. Have you conducted a national snapshot of what does the landscape look like, what programs may exist out there? From a research perspective, there may be a question of feasibility. What's the ramp-up time? If you've got partial components, what does it take a community center to ramp up effectively?"

NIEDERHUBER: "We've certainly done a lot of legwork, exploring options. We've tried to see what else exists. Some of the larger systems came to NCI to talk with us. The answer to your question is a resounding 'yes,' we've dug deep and spent time talking with center directors as well."

MOON CHEN JR., head of population science, UC Davis Cancer Center: "This is tremendous. I'm thrilled by the vision that you have of linking together a nationwide cohort that will enable us to do all these things. I really think this is a wonderful trans-NCI effort, too, where you've brought together CaBIG and disparities and surveillance. I want to commend you for the focus on disparities. To put 40 percent of the funding emphasis on disparities is tremendous."

LLOYD EVERSON, vice chairman, US Oncology Inc.: "I applaud your vision. It's ambitious, to say the least. It is the vision that our network of over 1,000 practicing oncologists try to emulate. It's very ambitious. I'd love to work with you. I'd be happy to help in any way I can. To give you an idea of the leverage you are proposing, your $9 million breaks out to about $1.5 to $2 million per site. We spend today in our small little network about $35 million on cancer research. It's a break-even proposition at best. There may be some leverage here, but it's not an uncostly endeavor."

NIEDERHUBER: "We don't know yet what we'll be able to spend per site, but clearly, this is a partnership. It will have to be a partnership. We think there are some important things we will bring as NCI that makes it worthwhile."

BRUCE CHABNER, clinical director, Massachusetts General Hospital Cancer Center: "I think this is a very interesting and challenging proposal. We've had some experience in the last couple of years trying to do this through an NCI-sponsored grant. It was called Overcoming Barriers to Recruitment of Minority Patients. We chose to do this with the Cambridge Hospital system, which is largely Hispanic, and found some unexpected challenges, which I think need to be anticipated, such as the need for a very strong program for translation so that patients understand what they are getting into. The real difficulty of putting patients on very complex protocols, such as the current phase I protocols that we are doing or try to do at our academic centers, are increasingly complex, with a lot of imaging, sample collection, bioassays of all sorts. In fact, our hospitals have had to set up separate translational research laboratories which are funded through the hospitals to accomplish this. What we've been able to do with Cambridge is put patients on phase II trials, and relatively simple trials.

"The other problem is finding the right trial for the right patient. We anticipated that every eligible patient would find a trial in our system of 400 clinical trials at our cancer center. It turns out that one in four finds an appropriate trial, because of eligibility requirements and all the other problems. I think there's a lot of thinking that has to go into the way that this is really going to be feasible on a larger scale. We have to particularly be able to match the trial to the expertise available locally."

EVERSON: "I would second what Bruce was saying. In the last year, we set up a phase I/early phase II network as part of our research program. Commitment locally, and not just in ideas, but in real dollars from that practice/hospital is absolutely key."

NIEDERHUBER: "I had some experience setting up phase II, what we called the Wisconsin Oncology Network. It was a little slow ramping it up and getting participation. Once I was able to get it going and get the private practices across the state involved, it

literally decreased our time to completion of a trial by 50 percent."

NCAB CHAIRMAN CAROLYN RUNOWICZ, director, Neag Comprehensive Cancer Center, University of Connecticut: "I think what you heard from the board was support with some concerns about some of the issues, but feasibility will hopefully iron those out."

A Randomized Trial Doomed Genta Accelerated Approval

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down Genasense (oblimersden sodium) in combination with fludarabine and cyclophosphamide as a treatment for chronic lymphocytic leukemia.

The committee agreed that Genasense improved complete responses and nodular partial responses by 10 percent. However, the clinical significance of this improvement was unclear, the committee said.

Moreover, the drug didn't qualify for accelerated approval since the sponsor, Genta Inc., had completed a randomized trial that failed to show improvements in survival, time to progression, or duration of response.

With a phase III trial showing no overall clinical benefit, the company was in no position to convince the committee that an improvement in CR and nPR could be reasonably likely to predict a clinical benefit, thereby making Genasense eligible for an accelerated approval.

Genta could have been better served by performing a less rigorous study, noted Susan O'Brien, a leukemia expert at M.D. Anderson Cancer Center, an investigator on one of the Genasense trials, and one of the company's presenters.

"I think we are penalizing the sponsor for the fact that they did a randomized trial," O'Brien said to ODAC. "Every drug that has been approved in leukemia so far has been approved based on response rate, mostly from single-arm trials. If this were a single-arm trial that showed a benefit in response, compared to historical data, nobody would be raising this issue of time to progression. It's only because this is a randomized trial where we have these two groups, that this would even come up."

The committee voted 7-3 against approval.

In a third action, the committee voted unanimously for approval of Fragmin (dalteparin sodium injection) for treatment and prevention of recurrence of venous thromboembolism in cancer patients. The drug is sponsored by Pfizer Inc. and is approved for indications that include use with abdominal and hip replacement surgery and the treatment of unstable angina.

In the course of reviewing the Fragmin supplemental new drug application, agency officials noted an imbalance in discontinuations due to deaths on the two arms of a randomized study that compared Fragmin to oral anticoagulants.

While study discontinuations due to death were at 17 percent for Fragmin, such discontinuations were at 7 percent for oral coagulants. Meanwhile, overall mortality was similar: 39 percent for Frangmin and 41 percent for oral drugs.

ODAC discussion revealed the cause of this imbalance. Patients receiving the oral drugs were typically taken off therapy days before their deaths, while patients receiving Fragmin typically remained on therapy until death.

Though Fragmin didn't increase survival, it reduced the risk of symptomatic, recurrent venous thromboembolism by 52 percent compared to oral drugs. The fact that the Fragmin application made it to ODAC points to the agency's determination to air afety concerns, agency officials said.

Abraxane: A Leap That Wasn't

Abraxane was approved for metastatic breast cancer after failure of anthracycline-containing combination chemotherapy in January 2005.

The approval was based on response rates demonstrated in a non-inferiority trial that compared Abraxane with an outmoded regimen of paclitaxel (The Cancer Letter, Jan. 14, 2005).

The drug was approved through section 505(b)(2) of the Food, Drug and Cosmetic Act, which applies to new dosage forms and delivery routes for previously approved drugs.

However, the company's application for the adjuvant indication in effect asks FDA to lower its approval standards for adjuvant therapy, said Richard Pazdur, director of the FDA Office of Oncology Products.

"Let's take a look at what's being asked for here in terms of efficacy," Pazdur said. "The only efficacy statement that is being made is that there is no scientific reason that Abraxane would be less effective than Taxol, which really equates to downgrading the efficacy standard to, 'There is no evidence that the drug is not effective.' Which is pretty low. If this goes through, why couldn't any drug that shows a survival advantage in metastatic disease say, 'You know, Dr. Pazdur, we have an improvement of survival in metastatic disease setting by 30 percent. Let's skip the adjuvant study. We

know we are going to be better. We will just do a safety study.' That's unreasonable."

Breast cancer patient advocates opposed the application.

"We want to make sure that inferior drugs don't start creeping into the standard of care," Helen Schiff, of the Center for Medical Consumers, said to the committee at the public hearing session. "We want to make sure that newly diagnosed women have the very best shot at preventing a recurrence an not dying of breast cancer. It is important to remember that therapy in the adjuvant setting is curative for some women. We want to increase the number who survive, not decrease them. The stakes are very high. Once a drug becomes a standard of care, it can be used as the comparator arm in a registration trial. This is an advocate's worst fear. If the drug in the comparator arm is inferior, you can end up replacing one inferior drug with another inferior drug."

Abraxane and Taxol aren't bioequivalent, Pazdur said. "Pharmacokinetics of total paclitaxel are different between the two drugs," he said. "Although the measurement of 'free' paclitaxel may provide a more accurate depiction of the relative pharmacokinetics of these two drugs, information on the comparative pharmacokinetics of free paclitaxel generated from these drugs is not known. Also, comparisons of the biodistribution of the drugs are not known. The two drugs have different formulations and different infusion rates. The two drugs have different toxicity profiles. The two drugs have different response rates in the metastatic setting."

FDA officials said either a superiority or a non-inferiority trial would be required for the drug's approval. However, the company argued that a convincing trial would be impractical.

Using one set of assumptions, Hudis said that a non-inferiority trial would have to enroll 8,644 participants, and a superiority trial would have to enroll 190,622. FDA officials and several ODAC members countered that a more conventionally sized trial of a few thousand high-risk patients, or, perhaps, a neo-adjuvant trial, could be convincing.

"We will exercise regulatory discretion and flexibility to assure that the trial can be done," said Pazdur. "Obviously, even Dr. Pazdur wouldn't be asking for a 190,000-patient trial. But the trial could be commensurate with other adjuvant trials that are being done."

Even a reasonably-sized trial would be unnecessary, objected ODAC member Michael Perry, an oncologist at the University of Missouri who ultimately cast the lone vote in support of the application.

"It's going to take a very selected population of patients, and it's going to take a long time, at least seven years," Perry said. "Add another two years to get it up. Seven years to get it done. Nine years from now, are we going to be interested in knowing whether Abraxane is the substitute for paclitaxel in the adjuvant setting of breast cancer? I sincerely hope not. I hope that we will have found something that will be better. We are not exactly rearranging deck chairs on the Titanic, but we are certainly rearranging something on some kind of a ship. I would like to see this drug approved so we can provide a reasonable alternative, and I would like to suggest that the manufacturer be asked to do a reasonably small but rapidly completed study to look at the safety, to make sure that there is no detriment to safety. A 7,000-patient study is simply irrational. You couldn't get the patients to sign up. You couldn't get the clinicians to say, 'Gee, here is a really exciting study, comparing Coke and Pepsi to see which is the dark and caffeinated cola.' There is no sex to this study. We ought to consider approving the drug and requiring the manufacturer to do a safety study of X number of patients, and go from there."

ODAC member Ronald Bukowski disagreed. "But the issue is not the safety, necessarily," said Bukowski, director of the Experimental Therapeutics Program at the Cleveland Clinic Foundation. "The issue is efficacy. And I don't see the data on efficacy that says that these drugs are the same."

NCI biostatistician Richard Simon said an enormous adjuvant trial may not be needed to answer the questions.

"It's very beneficial, if you were to do that kind of a study, to do it in a high-risk group of patients," said Simon, chief of the NCI Biometric Research Branch, who served as a voting consultant to the committee. "There are other kinds of evidence. For example, you could do a randomized trial in Stage III patients. And you could do it preoperatively. And you could actually take the tumor specimens and examine tissue levels of paclitaxel in patients who had received Taxol vs. the patients who had received [Abraxane]. You could take somebody who was going to do a large adjuvant trial who was going to use Taxol, and they were going to use some other kind of randomization to evaluate something, and you could do sub-randomization. If you wanted to be creative about it, there are a variety of things you could do to move us from the evidence that's presented. I actually view the response rate in a phase III metastatic disease study as meaningful, but not full-proof in terms of predicting whether that medication

would have the same effect in the adjuvant situation. I am sympathetic with Dr. Perry's point of view. I don't really want to see 5,000 patients randomized to answer this question alone, but at the same time, just having that comparison of metastatic response rates is not evidence of effectiveness in the adjuvant setting."

ODAC acting chairman Maha Hussain said a comparison of paclitaxel and Abraxane in adjuvant breast cancer is not trivial matter. "From my perspective, a study should be done," said Hussain, a prostate cancer expert at the University of Michigan. "I think it's to protect patients. It's good science. It's good medicine."

Hussain cautioned the agency against lowering the approval standards. "Maybe tomorrow some other drug comes in and says, 'I don't really have to do adjuvant trials anymore. I am showing an advantage in metastatic disease.'"

SIMON: "I am not satisfied with the evidence for effectiveness or safety of the drug in the adjuvant situation, but I don't think we are being entirely fair when we say that if we approve this, then any drug that shows some activity in metastatic disease setting would be approved in adjuvant. This is a little bit different. We have Taxol approved in the adjuvant setting. And we have some evidence that this drug delivered in this way at this dose has more anti-tumor effect than Taxol. So it's not really showing some effectiveness in metastatic disease setting will automatically justify approval in the adjuvant."

BUKOWSKI: "But on the other hand, there are data that suggest that they differ. I think we have to be quite cautious."

Iressa Haunts Genasense

In May 2004, as ODAC members were realizing the extent of their error in recommending approval of AstraZeneca's lung cancer drug Iressa, Genta staged its first presentation of Genasense, seeking the frontline metastatic melanoma indication.

Like Iressa, Genasense appears to help some individual patients, but its efficacy seems to elude measurement in populations of patients.

Thus, two years ago, melanoma patients who claimed to have benefited from Genasense filled the hall, and a phalanx of Congressional aides took up much of a front row. Yet, political muscle and testimonials didn't help. Following discussion that repeatedly returned to Iressa, the committee killed the application (The Cancer Letter, May 7, 2004).

Iressa was mentioned again on Sept. 6. "I sit here, I can't help but think about the story of Iressa in lung cancer, where there is no question there was a small but real benefit to a small number of patients, and it turns out that there are reasons why some patients may respond, and it seems to me that you have not demonstrated who actually is benefiting," said ODAC acting chairman Hussain. "As I sit down here and look at it, if you treat 100 patients, you are getting a benefit for only 10, and you are subjecting 90 to costs, physical and monetary."

Loretta Itri, Genta's president of medical development and chief medical officer, seemed eager to distinguish her company's drug from Iressa, the agent that has failed to demonstrate efficacy and has been placed in a restricted access program.

"The Iressa study was a single-arm study," Itri said. "This is a randomized trial, in which everyone agrees there was rigorous criteria and good comparison between the two arms of the study, so we are comparing apples and apples. Secondly, with Iressa, the responses were partial remissions…."

HUSSAIN: "I am not asking you to compare Iressa to your drug. What is clear is that like in the Iressa story, the number of patients who benefited is very small. Therefore, it would have been wise and advisable to look at who actually might benefit, so that one can spare the majority of patients toxic treatment that is futile. I am not comparing the studies; I am bringing an example of an agent that was approved based on at best very modest evidence of activity in a very difficult disease that had a much lower median survival, and yet we came later to find out that in fact there are only certain subsets of patients that are likely to benefit.

ITRI: "We could not know when we designed the study who would be the patients who would achieve the greatest benefit. But there is a clear pattern emerging. It's pretty clear to us that patients who retain their ability to respond to the combination chemotherapy—because Genasense works to enhance the activity of chemotherapy—it makes sense that patients who still are able to respond to chemeotherapy are going to be the ones who benefit most.

"We have a clear story emerging that patients who have relapsed and are not refractory to the combination therapy, the patients who have received relatively less chemotherapy are the ones who are most likely to benefit. That is why we are designing a confirmatory study in the upfront population, because it makes sense that in that population the response rate differences… If we can translate the 10 percent difference that we are seeing in the incredibly heavily pretreated population

into the upfront setting, then we have the possibility of affecting endpoints like progression-free survival."

Uncertain Efficacy vs. Certain Toxicity

The addition of Genasense to fludarabine and cyclophosphomide is associated with increased toxicities, Pazdur said. These include severe and serious adverse events, including nausea, vomiting, fever, fatigue, and bleeding. There was also a greater need for blood transfusions.

"Genasense administration requires an indwelling central venous access device for continuous intravenous infusion and an external infusion pump (or hospitalization) for seven days monthly," Pazdur said. "Infusion catheter-related complications occurred in 16 percent of the Genasense patients, including catheter infections and venous thromboses, compared to a 3 percent rate in the control arm."

M.D. Anderson's O'Brien said the toxicity was a minor issue.

"When you add Genasense to FluCy, it has more toxicity," O'Brien said. "In my mind, it's not that major. First of all, most of it is Grade 1 to II. If I add another drug to FluCy—and we've done it, let's say Rituximab—80 percent of those patients—will have an infusion reaction. They are severe about 5 to 10 percent, way more than on this trial. If I added another chemo onto FluCy, I would get way more myelosuppression and infection. So I want to put this in perspective of adding anything to this two-drug regimen. We add another drug, we buy some more toxicity, but relative to what we might get adding any other drug, I think that that's not very much."

The agency argued that Genasense wasn't eligible for accelerated approval.

"One of the issues that we have with this whole accelerated approval is the following: part of the accelerated approval process is designed for drugs where we don't have evidence of clinical benefit, and we are [relying] on single-arm study or on interim analysis of a randomized study to approve the drug on the surrogate endpoint we believe might be likely to predict clinical benefit," Pazdur said.

"The situation that we have here is a bit different," Pazdur said. "We have a completed randomized trial. It isn't an interim analysis of a randomized study. We have mature data which don't show an impact on TTP. What we have here is a dilemma that we have a completed study. There is no impact on TTP.

"How can we say that this endpoint is reasonably likely to predict clinical benefit?"

Cancer Death Rates Drop; Lower Rates In Latinos

U.S. cancer mortality continues to drop overall, maintaining a trend that began in the early 1990s, according to the "Annual Report to the Nation on the Status of Cancer, 1975-2003," released Sept. 6.

However, the rate of new cancers remains stable. The report is scheduled for publication in the Oct. 15 issue of Cancer.

The report includes comprehensive data on trends over the past several decades for all major cancers. It shows that the long-term decline in overall cancer death rates continued through 2003 for all races and both sexes combined. The declines were greater among men (1.6 percent per year from 1993 through 2003) than women (0.8 percent per year from 1992 through 2003).

Death rates decreased for 11 of the 15 most common cancers in men and for 10 of the 15 most common cancers in women. The authors attribute the decrease in death rates, in part, to successful efforts to reduce exposure to tobacco, earlier detection through screening, and more effective treatment, saying that continued success will depend on maintaining and enhancing these efforts.

"The greater decline in cancer death rates among men is due in large part to their substantial decrease in tobacco use," said Betsy Kohler, president of the North American Association of Central Cancer Registries Inc. "We need to enhance efforts to reduce tobacco use in women so that the rate of decline in cancer death rates becomes comparable to that of men."

Overall cancer incidence rates (the rate at which new cancers are diagnosed) for both sexes and all races combined have been stable from 1992 through 2003. Overall rates for men were stable from 1995 through 2003, while rates for women increased from 1979 through 2003. Notably, incidence rates for female breast cancer stabilized from 2001 through 2003, ending increases that began in the 1980s. Whether this first indication of a changing trend is real or a random fluctuation cannot be determined until data reporting in the next few years is complete. Also, the data suggest a small increase in the female lung cancer incidence rate from 1991 through 2003, which is a much slower rate of increase than in prior years.

Among women, incidence rates decreased for cancers of the colon, rectum, and uterus, ovarian, oral, stomach, and cervical cancers. Among men, incidence rates decreased for colon, rectum, stomach, oral, and lung cancer, but increased for prostate cancer, myeloma,

leukemia, cancers of the liver, kidney and esophagus.

Incidence rates for pancreatic cancer for men and women stabilized from 2000 through 2003, after decreasing for about 16 years. Among women, the rates for non-Hodgkin lymphoma, melanoma, leukemia and cancers of the lung, bladder, and kidney have been increasing since at least 1975. Thyroid cancer incidence rates among women have increased since 1981. The rate increased 2.2 percent per year from 1981-1993. The rate then increased 4.6 percent per year from 1993 to 2000. From 2000 to 2003, the rate increased 9.1 percent per year. These rising trends are likely explained in part by changes in medical surveillance, but may also be a result of changes in risk factors.

The report includes a special section on cancer among U.S. Latino/Hispanic populations, the largest growing ethnic group. The report finds that for 1999 to 2003, Latinos had lower incidence rates than non-Hispanic whites for most cancers, but were less likely to be diagnosed with localized stage disease for cancers of the lung, colon and rectum, prostate, female breast, and cervix. However, Latino children have higher incidence rates of leukemia, retinoblastoma, osteosarcoma, and germ cell tumors than do non-Latino white children.

Several cancer sites with higher incidence rates in Latinos often have infectious origins: human papilloma virus in cervical cancer; Helicobacter pylori (H. pylori) in stomach cancer; and Hepatitis B and Hepatitis C in liver cancer. Relative to the NHW population, the proportion of cases for specific cancers, in relation to all cancer sites combined, varied among four Latino groups (Mexican, Puerto Rican, Cuban, and South/ or Central American).

"Information in this report about lower Latino cancer rates is very encouraging but also points to the urgent need to educate people about the ways to reduce their cancer risk and keep rates such as these as low as possible," said NCI Director John Niederhuber.

The annual report is a collaboration among the North American Association of Central Cancer Registries, NCI, ACS, and the Centers for Disease Control and Prevention.

"We are continuing to make progress in our fight against cancer," said CDC Director Julie Gerberding. "However, we can't become complacent. We must continue to fight to ensure that resources are available to address the importance of prevention, screening, and early detection, and promoting healthy behaviors which are proven strategies to reduce the burden of cancer."

The report is available at www.interscience.wiley.com/cancer/report2006.

In Brief:

Oncology Nursing Society Selects New Chief Executive

PAULA TRAHAN RIEGER was named chief executive officer of the Oncology Nursing Society.

Rieger, senior director for international affairs at the American Society of Clinical Oncology, will join ONS in early November.

"Paula has a great depth of knowledge and is highly respected in our field. I welcome her and look forward to working with her to ensure a smooth transition," said Pearl Moore, who will retire in January, after 25 years as CEO of the society, which has a membership of 33,000 registered nurses and other healthcare professionals.

Rieger spent more than 20 years at the University of Texas M.D. Anderson Cancer Center as a nurse practitioner in the Department of Clinical Cancer Prevention. She received her master of science in nursing degree from the University of Texas Health Science Center and a bachelor of science in nursing degree from the University of California, Los Angeles. She earned a bachelor of science in biology and completed studies as a nurse practitioner at the University of Texas Health Science Center. She earned professional certifications as an advanced oncology nurse from the Oncology Nursing Certification Corp. and as an adult nurse practitioner from the American Nurses Credentialing Center.

Rieger served on the ONS Board as secretary and on the ONS Foundation Board from 1995-1998. She completed a two-year term as president of ONS in April 2002.

"I am excited at the prospect of continuing the vision of leading the transformation of cancer care," Rieger said. "I look forward to working together with the board, staff, and our members to make sure that nursing has input into decisions that impact the delivery of care to patients. We will continue to expand nursing research as a foundation for evidence-based practice and focus our efforts on attracting and preparing the oncology nursing workforce for the future."

In the Cancer Centers:

WINSHIP CANCER INSTITUTE at Emory University received $7.9 million P01 grant from NCI for lung cancer research. The Georgia Cancer Coalition will provide additional funding for the project. The grant is built around four scientific projects, which are supported by three core laboratory facilities. The grant team includes 40 researchers, clinicians, fellows, and technicians from 10 departments in the Emory Woodruff

Health Sciences Center. **Fadlo Khuri**, associate director of the Emory Winship Cancer Institute, is director and co-principal investigator on the grant. **Haian Fu**, associate professor of pharmacology, School of Medicine, is co-principal investigator. In addition to Khuri, five other researchers involved in the P01 have received grant support from the Georgia Cancer Coalition as Distinguished Cancer Clinicians and Scholars. They are: **Otis Brawley**, associate director at Winship; **Wei Zhou**, assistant professor; **Shi-Yong Sun**, assistant professor; **Dong Shin**, professor; and **Leland Chung**, professor of Urology. Shin and Chung have served as advisors. . . . **LOMBARDI CANCER CENTER** at Georgetown University has received a $6.5 million gift from the Robert M. Fisher Memorial Foundation Inc. to establish the Jess and Mildred Fisher Center for Familial Cancer. The donation would expand both clinical and research programs, allow more research on genetic predisposition to cancer, provide increased clinical trial opportunities and evaluate and treat more patients. Of the gift, $1.5 million will endow the Cecilia F. Rudman Arts and Humanities Program Fund, substantially expanding the reach and scope of the Lombard arts therapy program. . . . **UNIVERSITY OF CALIFORNIA DAVIS** Cancer Center has purchased a $3-million tomotherapy machine. The machine combines a high-resolution CT scanner to a sophisticated linear accelerator, allowing doctors to visualize a tumor and apply radiation at the same time, with enhanced precision and higher radiation doses, said **Srinivasan Vijayakumar**, professor and chairman of radiation oncology. . . . **CANCER THERAPY & RESEARCH CENTER** of San Antonio hired three staff members, said **Karen Fields**, president and CEO. **John Sarantopoulos** has joined the center as medical oncologist specializing on dermatologic and urologic malignancies. He also will serve as a clinical investigator in the Department of Clinical Research at the CTRC Institute for Drug Development on clinical, pharmacokinetic, and preclinical investigations of new anticancer agents. **Alain Mita** is a medical oncologist and clinical investigator. He will care for patients in the medical oncology and multidisciplinary clinics and serve as principal investigator for phase I and phase II studies. **Monica Mita** joined the staff as a medical oncologist and clinical investigator. . . . **JOHANNES VIEWEG**, associate professor of urology and immunology and vice chief of research, Division of Urology, Duke University, was named founding chairman of the new Department of Urology at the University of Florida. He is affiliated with the Shands Cancer Center of UF. His research interests include the development of early clinical testing of immunotherapies and treatments for genitourinary tract, including prostate cancer. Ten scientists and administrative staff made the move with Vieweg. . . . **DAVID DAVIS,** of Childrens Hospital Los Angeles, was named clinical nursing director for Pediatrics at City of Hope. His work is in bone marrow transplantation and oncology, said **Larry Kidd**, vice president of patient care services and chief nurse executive. . . . **MEMORIAL SLOAN-Kettering Cancer Center** has created the molecular diagnostics service within the Department of Pathology and named **Marc Ladanyi** as the first chief. The service provides state-of-the-art molecular genetic and cytogenetic testing for patient care at Memorial Hospital. The service integrates the functions of three entities: the laboratory of diagnostic molecular pathology, the laboratory of clinical cytogenetics, and the laboratory of diagnostic molecular genetics. Ladanyi, a molecular pathologist joined MSKCC in 1993. Also, **Dan Littman** of New York University Medical Center, was appointed member of the immunology program in the Sloan-Kettering Institute and named the inaugural incumbent of the Alan N. Houghton Chair. . . . **JOSE DIAZ** was named director of pathology and director of the molecular oncology targeted therapy program, Institute for Drug Development, at Cancer Therapy & Research Center. . . . **WILLIE UNDERWOOD** was appointed assistant professor of urology, member of the genitourinary oncology multidisciplinary team, and research scientist for the communication and behavioral oncology subprogram at Barbara Ann Karmanos Cancer Institute. Underwood was at University of Michigan and the VA Medical Center in Ann Arbor. . . . **NEVADA CANCER Institute** added to its leadership and faculty positions. **Sandra Murdock** was named president and chief operating officer. She was deputy director for administration and chief operating officer at Winship Cancer Institute at Emory University, where she also was professor of hematology and oncology and assistant professor of health policy and management. **Heather Murren** will retain the title of CEO at NVCI. **Lin-Chi Chen** was appointed medical oncologist. Chen was a medical oncology fellow at Memorial Sloan Kettering Cancer Center. **Ronald Fiscus** was named director of cancer molecular biology, basic science. He was head of molecular and cellular gerontology, Center for Gerontology and Geriatrics at the Chinese University of Hong Kong. Fiscus also was professor in the Department of Physiology, faculty of medicine at CUHK and head of the cardiovascular research group, Department of Physiology, and faculty of medicine at CUHK. **James Symanowski** was named head of biostatistics. He

was senior research advisor of statistics at Eli Lilly and Co. where he oversaw early-phase investigational drugs through post-marketing products. He also led statisticians through product development for Alimta, and Gemzar. Also, **Nicholas Vogelzang**, director of Nevada Cancer Institute, was named chairman of the board of directors for the Mesothelioma Applied Research Foundation. He has worked on mesothelioma clinical trials, and led the clinical trial of Alimta, the first drug approved by FDA specifically for the disease. Vogelzang succeeds **Roger Worthington**, original chairman and founder of the foundation. Vogelzang has served six years on the board.

Funding Opportunities:

Prevention Research Grants

The Cancer Research and Prevention Foundation offers two-year grants of $80,000. Funds are awarded twice a year. The application deadlines are Feb. 28 and Sept. 14.

Funds will be awarded only to institutions or organizations that do not accept direct funding from the tobacco industry.

The issue of relevance to cancer prevention must be convincingly addressed in the application. Researchers need not be U.S. citizens. However, research must be primarily conducted in the U.S.

Complete application information can be found at www.preventcancer.org/research/guidelines.cfm.

Program Announcements

PAR-06-511: NCI Cancer Education and Career Development Program. R25. Full text: http://grants.nih.gov/grants/guide/pa-files/PAR-06-511.html. Inquiries: Dorkina Myrick, 301-496-8580; myrickd@mail.nih.gov.

PAR-06-505: Specialized Programs of Research Excellence in Human Cancer for the Year 2007. P50. Letters of Intent Receipt Date: Dec. 23, April 22, Aug. 21. Application Receipt Date: Jan. 23, May 22, Sept. 21. Full text: http://grants.nih.gov/grants/guide/pa-files/PAR-06-505.html. Inquiries: Jorge Gomez, 301-496-8528. Gomezj@mail.nih.gov.

PA-06-510: Exploratory/Developmental Grant for Clinical Studies of Complementary and Alternative Medicine. R21. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-510.html. Inquiries: Wendy 301-435-7980, smithwe@mail.nih.gov.

PA-06-512: Mentored Clinical Scientist Research Career Development Award. K08. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-512.html. Inquiries: David Eckstein, 301-496-8580; eckstein@mail.nih.gov.

PA-06-522: Networks and Pathways Collaborative Research Projects. R01. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-522.html. Inquiries: Karl Krueger, 301- 594-1044, kruegerk@mail.nih.gov.

PAR-06-520: Dissemination and Implementation Research in Health. R03. Letters of Intent Receipt Date: 08/22/, 04/24, 2007, 12/28, 08/25/2008, 4/22/2009. Application Submission/Receipt Date: 09/22, 05/24/2007, 01/24/2008, 09/24, 05/22/2009.Full text: http://grants.nih.gov/grants/guide/pa-files/PAR-06-520.html. Inquiries: Jon Kerner, 301-594-7294, kernerj@mail.nih.gov.

PAR-06-521: Dissemination and Implementation Research in Health. R21. Full text: http://grants.nih.gov/grants/guide/pa-files/PAR-06-521.html.

PA-06-533: Functional Links between the Immune System, Brain Function and Behavior. R21. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-533.html. Inquiries: Paige McDonald, 301-435-5037; mcdonalp@mail.nih.gov.

PAR-06-534: Innovations in Biomedical Computational Science and Technology Initiative. STTR R41/R42. Application Submission Date: Sept. 24. Full text: http://grants.nih.gov/grants/guide/pa-files/PAR-06-534.html. Inquiries: Peter Lyster, 301-451-6446; lysterp@mail.nih.gov.

PAR-06-535: Innovations in Biomedical Computational Science and Technology Initiative. STTR R43/R44. Application Submission Date: Sept. 24. Full text: http://grants.nih.gov/grants/guide/pa-files/PAR-06-535.html.

PAR-06-540: Cancer Education Grants Program. R25. Full text: http://grants.nih.gov/grants/guide/pa-files/PAR-06-540.html. Inquiries: Lester Gorelic, 301-496-8580; gorelicl@mail.nih.gov.

PA-06-542: Mechanisms, Models, Measurement, & Management in Pain Research. R21. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-542.html. Inquiries: Ann O'Mara, 301-496-8667; omaraa@mail.nih.gov.

PA-06-543: Mechanisms, Models, Measurement, & Management in Pain Research. R03. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-543.html.

PA-06-544: Mechanisms, Models, Measurement, & Management in Pain Research. R01. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-544.html.

RFAs Available

RFA-HL-07-007: Bioengineering Approaches to Energy Balance and Obesity. R21. Letters of Intent Receipt Date: Nov. 24. Application Submission/Receipt Date: Dec. 22. Full text: http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-07-007.html. Inquiries: Sharon Ross, 301-594-7547; sr75k@nih.gov .

RFA-EB-06-003: Technology Development of Image-Guided Interventions: Phase I. R21. Letters of Intent Receipt Date: Sept. 25. Application Submission/Receipt Date: Oct. 23. Full text: http://grants.nih.gov/grants/guide/rfa-files/RFA-EB-06-003.html. Inquiries: Keyvan Farahani, 301-496-9531; farahank@mail.nih.gov.

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