THE CANCER LETTER

Vol. 34 No. 6
Feb. 15, 2008

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Roche Reports New Avastin Results As FDA Mulls Breast Cancer Indication

By Paul Goldberg

In a move that could be compared to introducing new evidence just as the judge clears his throat to read the verdict, the Swiss pharmaceutical company Roche earlier this week released the results of a trial of Avastin and Taxotere in front-line metastatic breast cancer.

Sometime before Feb. 23, FDA is expected to announce its decision on the addition of Avastin (bevacizumab) to taxane therapy for the disease. The decision would likely set a precedent, since the case for Avastin's approval is based on progression-free survival in a setting where the agency has historically demanded an improvement in overall survival.

On Feb. 12, Roche said its 736-patient placebo-controlled phase III trial

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NIH News:

Bias Against Young Investigators Threatens To "Deprime The Pump," Zerhouni Says

By Kirsten Boyd Goldberg

The average age of first-time NIH grantees has risen significantly in the past 26 years, a disturbing trend that the institute's funding policies should begin to address, NIH Director Elias Zerhouni said last week.

In 1980, the average age of first-time grantees was 36 for Ph.D.'s and 38 for M.D.'s. By 2005, that had risen to 42 for Ph.D.'s and 44 for M.D.'s, Zerhouni said.

Over the same time period, the average age of all NIH grantees has increased, from 39 in 1980 to 51 in 2006. Using actuarial projections, Zerhouni calculated that by 2020, there will be significantly more NIH principal investigators over age 68 than those under age 38.

These demographic trends are "eye-opening," and NIH policy-makers and advisors should begin to think about the long-term implications, Zerhouni said to the National Cancer Advisory Board Feb. 5. It's the younger investigators on their first grant or first renewal who usually explore new scientific areas and push the boundaries in areas such as epigenomics and proteomics, Zerhouni said.

"This is where new ideas emerge. Unless we establish policies now, what we might end up with is a pump that will be deprimed," Zerhouni said. "We will end up with a real loss of national competitiveness in our ability to sustain science."

Also, while the number of R01 investigators remains about the same

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Is PFS Good Enough? AVADO Results Consistent With E2100

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showed that Avastin produced an improvement in PFS in a trial very similar to one currently before the agency.

Will FDA consider the new results before rendering its decision? Will the agency even care about a stronger case based on PFS, or will it continue to demand survival? And since the agency accepts delay in progression in all other breast cancer indications, how would it explain demanding survival in the front-line metastatic indication?

ODAC Opinion Split

FDA will not be able to hide behind the back of the Oncologic Drugs Advisory Committee in reaching the verdict. At a meeting Dec. 5, the agency's clinical advisors came to a split recommendation on two questions. The vote was 5-4 against approval, not enough to offer a political mandate in either direction (The Cancer Letter, Dec. 14, 2007).

In discussion, with no vote taken, the committee appeared to be similarly split on the question of acceptability of PFS as a measure of clinical benefit.

Genentech and Roche announced that the latest trial, called AVADO, met its primary endpoint of prolonging PFS in patients who had not received prior chemotherapy for their locally recurrent or metastatic HER2-negative breast cancer.

Genentech is partially owned by Roche, and the two companies are co-developing Avastin.

"It had to be a pretty positive result for it to show up in the first planned interim analysis," said George Sledge, professor of pathology and laboratory medicine at the Indiana University School of Medicine and chairman of the breast committee of the Eastern Oncology Cooperative Group, which designed and conducted the E2100 trial that forms the basis of the approval application before FDA.

"That suggests that the AVADO results probably would be consistent in rough terms with the results of E2100 in terms of PFS," said Sledge. "If you go back to ODAC and ask, what are the two basic criticisms of E2100 at ODAC, the one criticism was, we don't trust E2100 because it didn't have a placebo control or an independent review panel. And the second criticism was, we don't like PFS as an endpoint in front-line metastatic breast cancer.

"So, the former, presumably, with this trial is wiped away. AVADO is highly consistent with E2100. This is biological reality that bevacizumab prolongs progression free survival in breast cancer when you combine it with a taxane in the front-line setting.

"The second point, which is PFS vs. overall survival, borders on being a theological dispute," Sledge said. "If you believe in your heart of hearts that only drugs that improve overall survival should be approved in metastatic breast cancer, then the power of these trials for overall survival probably would require two to three times as many patients as were enrolled in these trials. That's a very high bar. If drug companies are required to pass that bar to get a drug approved in front-line metastatic breast cancer, they will probably stop doing studies in front-line metastatic breast cancer."

FDA Given PFS Data, Genentech Says

Genentech spokesman Edward Lang said FDA has been given data on PFS, the primary endpoint of the AVADO study. Also, the agency has been given data on secondary endpoints, which include the overall survival, response rate, time to progression and quality of life.

"We also shared the initial safety information," Lang said. "The overall survival data are still immature at this point, and patients will continue to be followed." The survival data from AVADO would be expected in mid-2009, Lang said.

Though he hasn't seen the AVADO results, Sledge said the agency was likely given the data presented to the trial's data and safety monitoring board. "When you take an early look like that, you have to pass O'Brien-Fleming boundaries," he said.

THE CANCER LETTER

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Subscriptions/Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
General Information/FAQ: www.cancerletter.com

Subscription $375 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

A mature trial has to have a p-value of less than 0.05 to reach statistical significance. On a first look, the p-value usually has to be well less than 0.01, biostatisticians say.

The DSMB would have gone through toxicity data, likely finding little that would appear unexpected, Sledge said. "The overall survival would probably not be very mature at this point," and it would be unlikely that a negative trend in survival would be observed, he said. "It's hard to imagine that they would recommend release of data if there were any evidence of increased mortality."

Unlike the open-label E2100 trial, AVADO was a double blind and placebo-controlled. Patients were randomized to two doses of Avastin with chemotherapy versus chemo alone.

In AVADO, the doses were 15 mg/kg and 7.5 mg/kg every three weeks. In E2100, the Avastin dose was 10 mg/kg every two weeks in the experimental arm.

The taxane doses in the two trials were similar, and the higher dose of Avastin in AVADO was similar to the dose in E2100, Sledge said.

"Weekly paclitaxel and three-week docetaxel are probably reasonably similar in terms of activity in breast cancer," he said. "There are differences in toxicity between the two, but there aren't huge differences in activity in terms of breast cancer. Their high dose and the dose in E2100 are in essence the same thing. Their lower dose, 7.5 mg/kg basically is half the dose of what was used in E2100."

According to the company, AVADO shows that both doses were superior to placebo. This could be consistent with another Avastin trial, AVAIL, conducted in non-small cell lung cancer.

"If in AVADO both arms are pretty similar, and if in AVAIL both arms are pretty similar, then you have pretty compelling evidence from two major tumors that you can get by with a lower dose of bevacizumab," Sledge said.

AVADO allowed crossover to Avastin for the docetaxel alone arm at disease progression and at the discretion of the medical monitor. Data was collected on crossover. In E2100, data from Avastin crossover wasn't collected.

Arbitrary Distinctions?

"In the ideal world, a survival advantage should be required," Joanne Mortimer, professor at the Division of Medical Oncology & Experimental Therapeutics at City of Hope Comprehensive Cancer Center and an ODAC member who voted for approval of Avastin. "If that is not achieved, an improvement in disease free survival that is not achieved at a cost of toxicity compromising quality of life is desirable."

Many breast cancer experts say that it's unrealistic to set a separate standard for the front-line metastatic breast cancer setting.

"If you are allowing it in the second and third line setting in metastatic disease, why not allow it in the first-line setting?" said Eric Winer, director of the Breast Oncology Center at the Dana-Farber Cancer Institute and an unpaid consultant to Genentech, who took part in the ODAC presentation last December. "I think we make much too much of this difference between first and second-line therapy, and given the variability and the amount of adjuvant therapy that is administered, oftentimes a second-line patient may be actually less heavily pretreated than a first-line patient. The distinctions feel, at least in 2008, a little arbitrary to me."

The delay in progression is used in the adjuvant setting, where the stakes are especially high.

"The reason we use it in the adjuvant setting is that it takes so long to see an overall survival benefit, and there it is presumed that most of the time progression-free survival will translate to an overall survival benefit," Winer said. "Here, we actually do know in the ECOG trial that a substantial difference in PFS did not translate into a significant difference in overall survival."

In the second half of 2008, Genentech expects the results from another phase III clinical trial, RIBBON 1, which evaluates the 15 mg/kg every 3 week dose of Avastin in combination with anthracycline, taxane, or capecitabine chemotherapy for the first-line treatment of metastatic breast cancer.

Here again, the primary endpoint is PFS and overall survival is a secondary endpoint.

Great luck would be required to reach the overall survival endpoint in these studies, Sledge said. "I don't think it's feasible in this setting," he said. "Herceptin was an example of when Genentech got exceptionally lucky, because it had an overall survival advantage. It spoiled everyone. It was close, but it was an overall survival advantage."

With Avastin, "it took two-and-a-half, three years to accrue for E2100," Sledge said. "To say that we are going to require a trial two to three times as large to show an overall survival advantage, you are talking about front-line metastatic breast cancer trials that go on for six, seven, eight, nine years rather than two or three years. I don't view that as something that is going to move the field forward."

NIH News:

NIH Sets Floor Of 1,523 R01s For New Investigators In FY08

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no matter the level of the NIH budget, that's not true for new investigators, he said. There is a strong correlation between the number of new investigators and the NIH budget. When the budget is level or falls, funding for new investigators is disproportionally affected, he said.

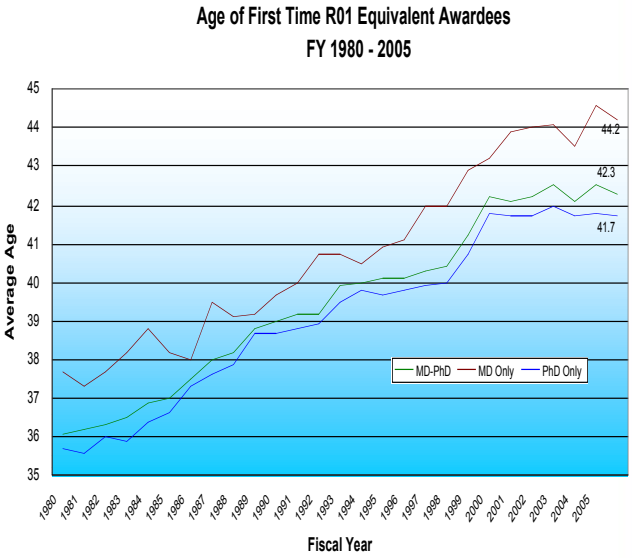
"There is a bias in the system that taxes the new investigators," Zerhouni said.

In 2005, NIH funded 1,683 new investigators, but the next year, the number dropped to 1,353. "That's why last year we agreed to maintain a floor of about 1,523 new investigators per year," he said. "We will continue the policy in '08, and we are asking advisory boards to be cognizant of the historical trends."

Zerhouni said he hopes to maintain a success rate of about 20 percent for new R01 grantees.

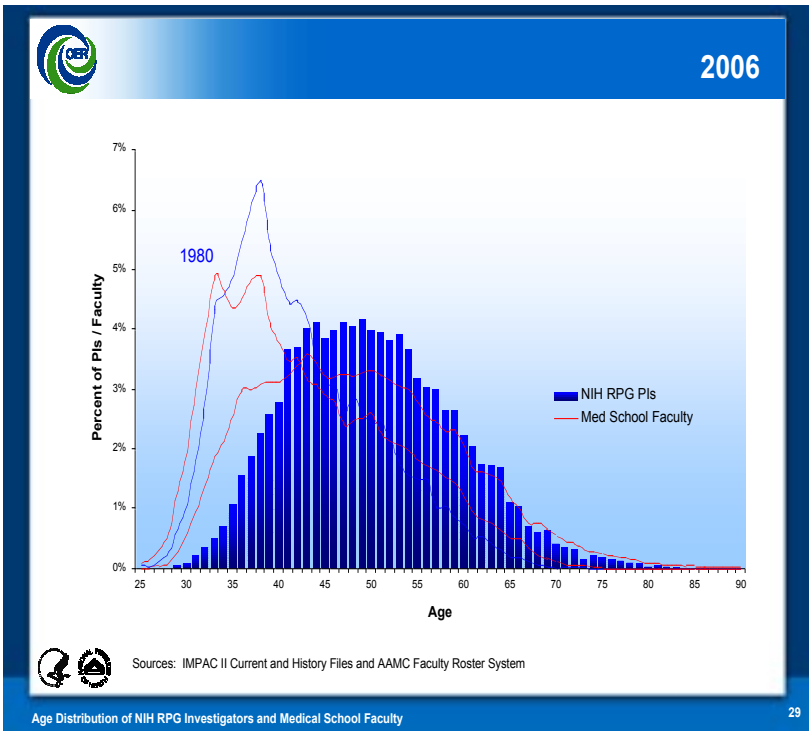
Zerhouni's data are "very disturbing," said Robert Weinberg, member of the Whitehead Institute for Biomedical Research, a biology professor at Massachusetts Institute of Technology, and director of the MIT Ludwig Center for Molecular Oncology.

"They are disturbing because the dynamism of basic biomedical research comes from the energetic, young, creative minds who are unafraid of taking chances and who possess unlimited energy and



unfettered imaginations," Weinberg said to The Cancer Letter. "By age of 40, much of this creativity and energy begins to peak, if not decline.

"We confront a future in this country in which we will have large numbers of graying researchers in laboratories," Weinberg said. "Their sheer numbers will give the illusion that our science remains dynamic and innovative, whereas the reality—which is often far harder to quantify—will be, sadly, much different. By then, we will have passed the baton of research leadership on to other countries and other societies that have addressed this problem successfully—how to ensure a large population of young people as central players in our research enterprise."



Young scientists are also taking longer to complete their training, Zerhouni said. The average age at which assistant professors are appointed at U.S. medical schools has risen from the mid-30s in 1972 to the late 30s in 2006.

Also, it's taking these scientists longer to get their first grant after their appointment.

NIH will award 10,100 grants in FY07, a number that will drop to 9,750 in FY08.

NIH awarded 265 Director's Bridge Awards in FY07 for "at-risk" investigators, Zerhouni said. These include those seeking their first renewal, and established investigators with less than $400,000 in other financial support.

NIH, EPA To Collaborate On Chemical Safety Testing

NIH and the Environmental Protection Agency have signed an agreement to collaborate on chemical safety testing.

Two NIH institutes have formed a collaboration with the EPA to use the NIH Chemical Genomics Center's high-speed, automated screening robots to test suspected toxic compounds using cells and isolated molecular targets instead of laboratory animals. The collaboration would generate data more relevant to humans, expand the number of chemicals tested, and reduce the cost and number of animals involved in testing, the federal scientists said.

"This research collaboration has the potential to make crucial discoveries that will protect the public health by identifying and understanding chemical toxicants to which people are exposed." said NIH Director Elias Zerhouni.

A five-year Memorandum of Understanding describes a collaboration between the National Toxicology Program at the National Institute of Environmental Health Sciences, the high-throughput technology at NCGC, managed by the National Human Genome Research Institute, and EPA's recently formed National Center for Computational Toxicology.

The MOU provides for sample and information sharing necessary to more rapidly and effectively identify chemicals that might pose possible risks to the health of humans and animals and to the environment. It addresses opportunities for coordination in four basic areas related to achieving the toxicant testing goals, including: identification of toxicity pathways; selection of chemicals for testing; analysis and interpretation of data; and outreach to scientific and regulatory communities. The collective budget is yet to be determined.

The collaborative research program is outlined in a jointly authored Science paper published Feb. 15. The co-authors—Francis Collins, NHGRI director; George Gray, assistant administrator for EPA's Office of Research and Development which houses the NCCT; and John Bucher, NTP associate director—describe the possibility of shifting from reliance on animal testing to biochemical- and cell-based assays, as well as those using lower organisms, such as zebrafish and roundworms.

"A central component of federal effort will explore the use of high-throughput screening assays in toxicology," Collins said. "Such assays allow for the testing of thousands to hundreds of thousands of chemicals a day to determine their possible toxic effect."

NCGC is part of a larger Molecular Libraries Imaging Program within the NIH Roadmap for Medical Research. It was designed to advance research on molecules from which most medicines marketed today are derived.

"We now are seeing tools newly available to us for chemical genomics research deployed for greater refinement, speed and capacity in chemical toxicity screening," Collins said.

"The experimental and computational expertise required to transform toxicology is an enormous undertaking and too great for any of our existing organizations to accomplish alone," said NTP's Bucher. "This collaborative approach allows us to draw on our individual strengths and establishes a long-term, multiple U.S. federal agency commitment."

NTP will contribute thousands of compounds for testing. NTP's animal toxicology expertise will be utilized, along with a large database of the chemicals' effects on animals, with which the new cell-based data will be compared.

"As our detailed research strategy continues to develop, we will welcome the participation of other federal partners, as well as interested public and private sector organizations, to make this vision of 21st century toxicology a reality," said EPA's Gray.

The EPA's ToxCast program will use advances in computers, genomics and cellular biology to speed up toxicity testing and enhance capacity to screen new compounds.

Smoking's Effects On Genes May Play Role In Lung Cancer

NCI researchers have shown that smoking affects the way genes are expressed, leading to alterations in cell division and regulation of immune response.

Notably, some of the changes in gene expression persisted in people who had quit smoking many years earlier. The findings appeared in the *Feb. 20* issue of PLoS ONE.

"Smoking, we are well aware, is the leading cause of lung cancer worldwide," said NCI Director John Niederhuber. "Yet, a mechanistic understanding of the effects of smoking on the cells of the lung remains incomplete. This study demonstrates an important piece of this complicated puzzle. Greater understanding of

the genetic alterations that occur with smoking should provide greater insight into the development of cellular targets for treating, and possibly preventing, lung cancer."

"We were able to look at actual lung tissue, tumor and non-tumor, taking into account the differences by gender, verifying the smoking status by measuring levels of cotinine, a metabolite of nicotine, in participants' plasma, and confirming results in independent samples," said Maria Teresa Landi, in NCI's Division of Cancer Epidemiology and Genetics, the first author of the study report.

To investigate the effects of smoking on gene activity in lung tissue, the researchers examined the gene expression profiles in early-stage lung tumors and non-tumor lung tissue of smokers, former smokers, and people who had never smoked cigarettes.

Gene expression was measured in 58 fresh-frozen tumor and 49 fresh-frozen non-tumor samples from 74 participants of the Environment And Genetics in Lung cancer Etiology (EAGLE) study, a large lung cancer study that was conducted in the Lombardy region of Italy.

Adenocarcinoma tumor samples were evaluated in this study because adenocarcinoma is the most common type of lung cancer, and it occurs in both smokers and people with no history of smoking. The participants were 44 to 79 years of age, and 28 were current smokers, 26 were former smokers, and 20 had never smoked.

The researchers also obtained detailed medical information about the participants (for example, whether individuals had previous lung diseases or chemotherapy) and biochemically confirmed participants' smoking status.

Using microarray techniques, which allow researchers to look at the activity of thousands of genes simultaneously, they identified 135 genes that were differently expressed in tumors of smokers vs. people who had never smoked. Among these genes, 81 showed decreased expression and 54 showed increased expression in tumor tissue.

Most of the genes showing significantly increased expression, e.g., TTK, NEK2, and PRC1, are involved in cell cycle regulation and mitosis. The cell cycle is a step-wise sequence of events in which a cell grows and ultimately divides to produce two progeny, or daughter, cells.

During the cell cycle, the chromosomes of the parent cell are duplicated and then, in a step called mitosis, divided equally between the daughter cells, ensuring that each daughter cell inherits a complete set of chromosomes. The cell apparatus responsible for the proper division of chromosomes is called the mitotic spindle.

"Our results indicate that smoking causes changes in genes that control mitotic spindle formation," said Jin Jen, in NCI's Center for Cancer Research, a senior author of the study report. "Irregular division of chromosomes and chromosome instability are two common abnormalities that occur in cancer cells when the chromosomes do not separate equally between the daughter cells. Therefore, changes in the mitotic process are very relevant in the development of cancer."

Several of the identified genes have been suggested in the past as potential targets for cancer treatment.

The researchers also found similar expression of many genes among current smokers and former smokers in tumor tissue. Several of these genes, such as STOM, SSX2IP, and APLP2, remained altered in participants who had quit smoking more than 20 years before the study. Therefore, smoking seems to cause long-lasting changes in gene expression, which can contribute to lung cancer development long after cessation.

Looking at non-tumor lung tissues, the team found decreased activity for 73 genes and increased activity for 25 genes in current smokers. The genes most affected by smoking play a role in immune response-related processes, possibly as a lung defense mechanism against the acute toxic effects of smoking. However, non-tumor tissues seem to be able to recover from the effects of smoking.

The researchers did not identify significant changes in the immune response-related genes in former smokers.

To gain a better understanding of the impact of smoking-related changes in gene expression on lung cancer survival, the researchers compared the overall gene expression smoking profile in lung tumor and non-tumor tissues with survival. They found that the altered expression of the cell cycle-related genes NEK2 and TTK in non-tumor tissues was associated with a three-fold increased risk of lung cancer mortality in smokers.

"Our data provide clues on how cigarette smoking affects the development of lung cancer, indicating that the very same mitotic genes known to be involved in cancer development are altered by smoking and affect survival. More studies are needed to confirm that the gene expression changes are due to smoking and affect tumor development or progression," said Landi. "If confirmed, these genes could become important targets for preventing and treating lung cancer."

In the Cancer Centers:

DFCI And Merck To Collaborate On Drug Targets And Therapies

DANA-FARBER CANCER INSTITUTE and Merck and Co. Inc. have established a collaboration to identify promising drug targets, and develop therapeutic candidates to reach those targets. The collaboration will involve faculty in DFCI's Center for Applied Cancer Science. **Lynda Chin** will serve as senior investigator in the CACS-Merck alliance.

Under the terms of the agreement, Merck will provide up-front and research support funding to the CACS as well as milestone and royalty payments upon market approval. The CACS will investigate drug targets using integrative and cross-species genomic analysis and stringent multi-level functional and clinicopathological validation testing. The CACS will work with Merck to shepherd the drug assay development of lead compound discovery and then work together to test these drugs in CACS's highly sophisticated model systems that closely replicate human disease.

"By actively facilitating communication, this new agreement represents an important advance toward true team science between Dana-Farber and one of world's the leading pharmaceutical companies," Chin said.

CACS faculty, under the direction of **James DeCaprio** and **Kenneth Anderson**, working with scientists from Merck Research Laboratories, to further evaluate tumor pathobiology and clinical outcomes to better pinpoint the tumor types most susceptible to the drug.

The CACS consists of team scientists and core laboratory facilities for identifying genetic alterations in cancer, pinpointing those alterations most crucial to tumor formation and maintenance, validating those targets in a wide range of cell and tissue cultures assays and sophisticated animal models, and, in the case of monoclonal antibodies, developing them into useful therapies. The CACS retains the right to develop its antibodies independent of the Merck collaboration.

* * *

STEVEN PIANTADOSI, director of the Samuel Oschin Comprehensive Cancer Institute at Cedars-Sinai Medical Center, was named the inaugural Phase ONE Foundation Endowed Chair at Cedars-Sinai Medical Center. The gift of the endowed chair will fund his directorship as well as cancer research at Cedars-Sinai. Piantadosi, who was named director in 2007, will lead initiatives that unite the Cedars-Sinai physicians and researchers from different specialties for clinical and scientific collaborations. Prior to joining Cedars-Sinai, Piantadosi was professor of oncology at Johns Hopkins University School of Medicine and director of biostatistics at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. . . . **KIMMEL CANCER CENTER** at Jefferson Medical College has made three appointments. **Leonard Gomella** was named interim medical director of the center. Gomella, the Bernard W. Goodwin, Jr. Professor of Prostate Cancer, also serves as the chairman of the Department of Urology and associate director of the cancer center. **Eric Knudsen**, former scientific director of the University of Cincinnati Barrett Cancer Center, was named deputy director, research. He succeeds **Renato Baserga**, professor of cancer biology at Jefferson. **Neal Flomenberg**, interim chairman and professor of medical oncology at Jefferson Medical College, was named deputy director, clinical science. He succeeds **Walter Curran Jr**., professor and chairman of radiation oncology.

In Brief:

Nevada Consortium Honors Sen. Reid For Biotech Support

SEN. HARRY REID (D-NV) will receive the inaugural Harry Reid Award for Biotechnology in Nevada from the Nevada Biotechnology and Bioscience Consortium on Feb. 18. "Having secured more than $100 million for Nevada universities, Sen. Reid has arguably been the State's leading supporter of higher education," said John Laub, president of the consortium. Also, the University of Nevada at Las Vegas College of Sciences will receive the organization award for biotechnology in Nevada. . . . **ONCOLOGY NURSING SOCIETY** announced 2008 awardees. **Agnes Glaus** is the recipient of the ONS International Award for Contributions to Cancer Care. Glaus, oncology nurse and nurse scientist at the Tumor Center ZeTuP, Center for Tumor-Prevention, Detection and Treatment in St. Gallen, Switzerland, is recognized for her pioneering leadership in cancer nursing and its role in supportive care of patients with cancer across Europe. **Ayda Nambayan**, curriculum and distance learning developer for the International Outreach Program at St. Jude Children's Research Hospital in Memphis, is the recipient of the Pearl Moore Making a Difference Award. The award recognizes her contributions to the oncology nursing profession at the local and regional levels. Her work includes End-of-Life Nursing Education Consortium trainer for Alabama and Tennessee and mentor for nurses from

Singapore to South Africa. **Carol Ferrans** was named Distinguished Researcher. She is professor, College of Nursing at the University of Illinois at Chicago and deputy director at the UIC Center for Population Health and Health Disparities. The honor recognizes her research contributions to the science and practice of oncology nursing. Her research work includes quality of life, including early detection and treatment, long-term survivorship, and end of life, as well as healthcare disparities. **Elizabeth Edwards** was named the ONS Public Service Award recipient for her public service and leadership in bringing cancer awareness and advocacy to the public. "Ms. Edwards has given a name and face to living with metastatic cancer," said Molly Loney and Deborah Mayer, her nominators. "She has created a new model of survivorship from which we can all learn and grow." Edwards is author of Saving Graces: Finding Solace and Strength from Friends and Strangers and the wife of former North Carolina **Sen. John Edwards**. The recipients will be honored in May at the ONS 33rd Annual Congress in Philadelphia.

Obituary:

STEVEN LEIBEL, the Ann and John Doerr Medical Director of the Stanford Cancer Center, died Feb. 7 of a heart attack while vacationing in Hawaii. He was 61.

Leibel came to Stanford in 2004 as the first medical director of the newly opened cancer center. He oversaw the roughly 350 cancer specialists at the center and played a key role in Stanford's successful effort to receive NCI designation for the cancer center.

"Steve was highly respected by his colleagues at Stanford as well as nationally and internationally. He will be deeply missed," said Philip Pizzo, dean of the School of Medicine. "Our hearts go out to his wife, parents and family—we have all lost a colleague, leader and friend."

Cancer center director Irving Weissman, said Leibel's expertise helped turn the center into a first-rate institution. "Throughout the development of the cancer center and especially in the recruitment of first-class clinicians and scientists, he showed extraordinary insight into the kinds of people who could advance our knowledge about the diagnosis and treatment of cancer," Weissman said. He added that while taking on administrative duties, Leibel maintained his interest in developing cancer treatments.

A San Francisco native, Leibel received his MD from UC-San Francisco where he also completed residency training in radiation oncology. He served on the faculties at Johns Hopkins University School of Medicine and UCSF before moving to New York in 1988 to join the Department of Radiation Oncology at Memorial Sloan-Kettering. He became chairman of that department in 1998.

While at Sloan-Kettering, Leibel helped developed extremely precise therapies for treating cancers of the prostate and the brain, using 3-D conformal radiation therapy and intensity-modulated radiation therapy. These techniques more precisely targeted tumors with high-dose radiation while sparing normal tissues. The result has been a significant improvement in cure rates for some cancers, particularly prostate cancer.

Richard Hoppe, professor and chairman of radiation oncology at Stanford, said the radiation technique Leibel advocated has since become standard care in prostate cancer. "He was one of the most widely respected radiation oncologists in the field," he said.

Hoppe added that Leibel's experience at three different cancer centers "gave him special talent in being able to bring people together."

Beverly Mitchell, deputy director of the cancer center, said Leibel "was committed to the very best cancer care and treatment at Stanford. His sudden loss comes as a great shock to all of us. We will miss him greatly and will do our best to carry on, as he would have wished, to expand upon what he has accomplished so well."

Leibel was president and chairman of the American Society for Therapeutic Radiology and Oncology, and received the society's gold medal. He was president of the American Board of Radiology, and was also on the board of Varian Medical Systems Inc.

Leibel is survived by is wife, Margy, of Palo Alto, Calif.; his parents, and his stepdaughter.

Funding Opportunities:

RFA-OD-08-001: Rare Diseases Clinical Research Consortia for the Rare Diseases Clinical Research Network. U54. Letter of Intent Receipt Date: July 20. Application Receipt Date: Aug. 20. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-OD-08-001.html. Inquiries: Rashmi Gopal-Srivastava, 301-402–4336; gopalr@mail.nih.gov.

RFP N02-CM-87001-45: Assistance to the Development Therapeutics Program. Response Due date: April 16. Full text: http://www.fbodaily.com/archive/2008/02-February/13-Feb-2008/FBO-01505416.htm. Inquiries: Kathy Giuliano, 301-435-3821, kg109o@nih.gov. or MaryAnne Golling, 301-228-4215, mg345x@nih.gov.

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