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Avastin Improves Lung Cancer Survival, Opens Options For New Combinations

By Paul Goldberg

Rapid innovation is shaking up the treatment of lung cancer.

In a little more than a year, scientists have demonstrated the benefit of adjuvant therapy for resected early stage disease, discovered the role of epidermal growth factor receptor mutations in lung cancer, and confirmed clinical efficacy of inhibiting the tyrosine kinase activity of the EGFR signaling pathway inside the cell to block tumor cell growth.

On March 13, Genentech Inc. and the Eastern Cooperative Oncology

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In Brief:

Pearl Moore To Retire As ONS CEO In 2007; Mack, Coats Join King & Spalding Law Firm

PEARL MOORE, CEO of the Oncology Nursing Society, announced her plans to retire on Jan. 31, 2007. Moore joined ONS as a member with 250 other nurses in 1975. In 1983, she became the organization's first executive director. Currently, she serves as chief executive officer of ONS, Oncology Nursing Certification Corp., ONS Foundation, and Oncology Education Services Inc.

During her tenure, ONS has grown to over 32,000 members with 220 chapters nationwide. Over 18,000 oncology nurses have earned professional certification through ONCC. Moore helped to raise $16 million to support the ONS Foundation Center for Leadership, Information and Research. ONS Foundation is the largest contributor to nursing research outside of NIH.

"The time has come," Moore said in announcing the move to ONS staff. "I love this job, but now is the right time. We are a strong organization because we have great employees, staff, and volunteers. We have developed a timeline and a process that will allow us to continue to provide excellent service to our members and further our mission."

"Pearl Moore is a CEO of great integrity and wisdom," ONS President **Karen Stanley** said. "The society is strategically poised to continue our advocacy efforts for nursing, for patients, and for the cancer community. Pearl's forethought and support have provided the board a solid plan for implementing a smooth succession."

* * *

FORMER SENS. Connie Mack (R-Fla.) and **Dan Coats** (R-Ind.) joined the law firm of King & Spalding as co-chairmen of the firm's Government

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Avastin Prolongs Survival In NSCLC; Details At ASCO

(Continued from page 1)

Group announced that a large randomized phase III trial demonstrated that the antiangiogenic agent Avastin (bevacizumab) increased survival in front-line therapy in advanced non-small cell lung cancer.

"This is the first time we have had a randomized trial showing that the addition of a targeted agent to chemotherapy improves survival in untreated metastatic NSCLC," said Alan Sandler, ECOG study principal investigator and medical director of thoracic oncology at Vanderbilt. "The results are statistically, but more importantly, clinically significant."

Unlike tyrosine kinase inhibitors Tarceva and Iressa, Avastin in this trial appears to have worked with chemotherapy. The Avastin results broaden discussion of targeted therapy in NSCLC beyond the other burning question: what went wrong with Iressa?

In 2003, Iressa received an accelerated approval for third-line NSCLC, but late last year, a randomized trial failed to demonstrate a survival advantage for its use. Iressa's sponsor, AstraZeneca, has stopped all promotion of the drug in the U.S., and urged doctors to steer new patients toward Genentech's drug Tarceva. At a meeting of the FDA Oncologic Drugs Advisory Committee earlier this month, agency officials indicated that they had no plans to pull Iressa off the market, but would likely revise its label.

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Founded Dec. 21, 1973, by Jerry D. Boyd.

"It's intriguing how this is going to sort out between the EGFR drugs, the newest chemotherapeutic agents that are out there, and now Avastin," said Kathy Albain, a lung cancer expert at Loyola University and a former ODAC member.

"How are these agents going to be combined and sequenced? All of this is going to be continued in the near future, as these data roll out for our scrutiny over the next few months."

Avastin Side Effects vs. Benefits

In the ECOG trial, patients who received Avastin in combination with paclitaxel and carboplatin had a median overall survival of 12.5 months, compared to patients treated with chemotherapy alone, who had a median survival of 10.2 months. The difference was statistically significant, ECOG and the company said.

The study enrolled 878 patients with advanced non-squamous, non-small cell lung cancer who had not previously received systemic chemotherapy.

Clinicians are eager to weigh Avastin's benefits against its toxicity, which includes fatal pulmonary hemorrhage. According to previously published phase II data, hemorrhages were more common in squamous cell NSCLC.

Patients with squamous cell NSCLC and patients with frank hemoptysis were excluded from the study, yet pulmonary hemorrhages were still observed with greater frequency on the Avastin arm.

According to Genetech, the hemorrhages occurred "infrequently," but were "more common in the patient group that received Avastin in combination with chemotherapy than in the patient group that received only chemotherapy."

"These results represent the first study combining a targeted biologic therapy with chemotherapy to show an overall survival improvement in the first-line non-small cell lung cancer setting, and the first time that any treatment has improved upon the standard, two-drug chemotherapy regimen in this disease," Genentech Senior Vice President and Chief Medical Officer Hal Barron said in a statement. "We plan to share these data with the FDA to discuss the possibility of filing a supplemental Biologics License Application for Avastin plus chemotherapy in first-line non-small cell lung cancer."

Vanderbilt oncologist Sandler said the ECOG study had one of the most aggressive safety mechanisms of any randomized phase III study.

"It was aggressively looked at in a very prospective manner," Sandler said. "We were essentially looking at

grade 3-5 hemorrhages almost as they occurred. There were early stopping rules that were written into the study. In fact, the study was stopped for interim analysis after the first 112 patients, because there was concern that the hemorrhages could potentially occur later, as opposed to early in treatment, and the study, of course, didn't stop. It was allowed to go."

The incidence of fatal bleeding was less than was seen in the earlier randomized phase II study, Sandler said.

"I think when all the data are available, the side effects will be acceptable, given the survival advantages," Sandler said, declining to discuss details on the incidence of toxicity. "It's important to allow the toxicity data to be analyzed and ultimately presented in a couple of months."

The rest will be released at the annual meeting of the American Society of Clinical Oncology May 13-17.

It appears that information on Avastin's survival advantage is reaching patients, and oncologists who treat lung cancer are starting to discuss using the drug off-label in NSCLC in some patients. Since the phase III Avastin study was performed by a cooperative group, the protocol—E4599—is readily available.

John Ruckdeschel, director and CEO of Barbara Ann Karmanos Cancer Institute, said he has started offering the drug as an option for patients with non-squamous disease, who want the most aggressive treatment available.

"If someone comes in and says, 'I don't want to be a part of a study, I don't care what it costs, I've got great insurance, I want to add everything I can, throw the kitchen sink,' I'll add Avastin to it," Ruckdeschel said.

Ruckdeschel views the Avastin finding as an incremental advance, and, like others in the field, he is concerned about the drug's toxicity. "I always warn patients that there is still this risk of fatal pulmonary hemorrhage with it," Ruckdeschel said.

Information released by ASCO and Genentech so far is insufficient to make a clear decision on Avastin, said Loyola oncologist Albain. "I think we have to be careful with the Avastin story, at least at this juncture," she said. "Patients with squamous cell carcinoma were excluded because of a significantly highter risk of hemorrhagic death in phase II studies. Also excluded were central neoplasms, so you are left with patients of extremely good performance status who have subsets of lung cancer, not the entire group.

"We are eagerly awaiting the ASCO presentation to see all of the data, and in particular, the press releases have indicated a significant increase of hemorrhagic complications, even though the patients at highest risk for those were excluded from the trial," Albain said.

"This is not going to be a drug for every patient with NSCLC in the advanced stage setting," Albain said. "It's clearly going to represent another advance in the field, but we need to see the toxicity data and the details of the inclusion criteria, and put those together with the actual survival outcome and adjustments in those survival outcomes for other known prognostic factors."

Sandler said follow-up trials would be required to test the drug in broader populations.

"For the patients eligible for E4599, the regimen of paclitaxel, carboplatin, and [Avastin] becomes the new standard," he said. "Potentially, this may be true with platinum-containing doublets, depending on FDA's decision. I think the next step is to see whether or not patients with squamous cell histology, and potentially brain metastasis may be able to tolerate, and benefit from the addition of Avastin."

Sandler said he would like to investigate using palliative radiation therapy to the primary tumor prior to using Avastin.

"It's possible that that group may benefit even more," he said. "And, of course, it can be tried in earlier stages of disease, combining it with chemo and radiation, and in the adjuvant setting."

Changes On the Chess Board

The Avastin finding, combined with the uncertain future of AstraZeneca's Iressa, establishes Genentech as the dominant force in the treatment of lung cancer, said Fadlo Khuri, Blomeyer Professor of Hematology and Oncology at Emory University Winship Cancer Institute.

"I think this means Tarceva is going to dominate in second and third line, and Avastin and chemo will dominate in front line," Khuri said. "I think this is going to mean that Genentech is the new superpower in lung cancer, with two targeted agents, one in front-line, one in second line.

"This makes Iressa's fall from grace all the more profound," he said.

Reacting to the Avastin announcement, Lehman Brothers downgraded OSI Pharmaceuticals sock and reduced its price target from $80 per share to $58 per share, pointing to "lackluster" sales of Tarceva and its potential competition with Avastin in second-line NSCLC.

Tarceva was developed by OSI and is being

evaluated and marketed by the company in an alliance with Genentech and Roche.

"While we have been optimistic regarding Tarceva expansion in second line NSCLC, feedback from clinicians suggests [Eli Lilly drug] Alimta has become a preferred agent," Lehman Brothers analyst Jim Birchenough wrote. "With Avastin's success in first-line NSCLC and potential for dosing through second line use with Alimta, we believe Tarceva's ling-term growth may be even more hampered."

In another reaction to the news on Avastin, Smith Barney, a division of Citigroup, noted that the availability of the Genentech drug may hamper the efforts by ImClone Systems Inc. to develop Erbitux for the lung cancer indication.

"In our view, the ongoing studies of Erbitux in front-line NSCLC might need to be amended if the fact that Avastin is not offered prevents timely patient enrollment," Smith Barney analyst Yaron Werber wrote. "Regardless of the enrollment rate, the Erbitux studies might prove to be outdated by the time data become available."

ASCO President David Johnson, head of the division of hematology and oncology and deputy director of the Vanderbilt Ingram Cancer Center, said lung cancer researchers are facing the challenge of sorting through the new array of options. "New drugs give us new opportunities to probe the tumor's behavior and biology," he said.

"I am confident that the next five to 10 years will bring even greater advances, provided we don't mess up and fall back into a pattern of doing the 'easy' studies," Johnson said. "This means that partnering with NCI, FDA and industry is critical. We should not be limited in the kinds of studies we can do simply because drug X is produced by one company, while drug Y is produced by another. Moreover, we cannot be seduced into carrying out a series of me-too trials. It is important to get the needed information and move on to the next important question."

Iressa and the Subsets

At an ODAC meeting March 4, FDA asked AstraZeneca to present the results of Trial 709, also known as ISEL, which failed to demonstrate a survival advantage for Iressa. AstraZeneca announced the preliminary survival results last December.

Though the committee wasn't asked to vote, discussion suggested support for the view that Iressa should not be given to new patients, because Tarceva has demonstrated a survival advantage.

Otis Brawley, an oncologist at Emory Winship Cancer Center and a member of ODAC, said Iressa has become a case study in how not to develop—and how not to approve—a targeted drug.

"I think we all owe [advocates and survivors] an apology, because the development of this drug has been mishandled," Brawley said at the ODAC meeting.

"It's been mishandled by AstraZeneca, it's been mishandled by this committee. I myself take some blame for that, because I voted for approval two years ago. The fact remains that this drug has been available for seven years, and we still have not figured out exactly how this drug should be used in the treatment of lung cancer. Perhaps, if we had held off in getting it available to people two or three years ago, those studies would have been done…

"In partial defense of those who have mishandled the development of this drug, including myself, this is one of the first of the targeted therapies to come along. Maybe we can learn from our mistakes and go forward."

According to data presented by AstraZeneca, patients who never smoked had higher survival on Iressa, compared to placebo. In smokers or former smokers, there was no difference between the groups. Also, patients of "Asian origin" who got Iressa had higher survival, compared to those who got placebo, the company said. In other populations, there was no difference between the groups.

According to the company, the "Asian" category excludes patients of Indian origin.

AstraZeneca is conducting a retrospective study of a potential association between the patients' EGFR expression and Iressa's efficacy. According to the Tarceva trial, that drug prolonged survival in the EGFR-positive subgroup. Results from AstraZeneca's analysis of the EGFR expression study were expected to be available by late March, the company said at the ODAC meeting.

Another retrospective look focuses on a specific mutation in the EGFR gene, which may correlate with response to Iressa. That analysis should be available in June, the company said.

However, in addition to being retrospective subset analyses, these studies will be hampered by the fact that tumor samples were collected from 500 of the 1,692 patients, who were randomized 2:1 to receive Iressa or placebo. Usually, about a third of tumors collected in trials are judged inadequate or unusable.

At the ODAC meeting, several committee members noted that the "Asian" subset was not clearly

defined.

"We live in the U.S. and have definitions of ethnicity that I am not sure are clear," said ODAC member Maha Hussain, an expert in urologic oncology at the University of Michigan. "I was born in Baghdad. I consider myself Asian. So does that word apply to me? I would not consider a Japanese person equal to Vietnamese equal to Chinese equal to Indian, Pakistani, Afghani, and on… I think those populations have to be very clearly defined beyond that 'Asian' ethnic group."

Brawley agreed. "There are a number of studies that have done a number of subset analyses," he said. "I've made my career, by the way, by saying we should not do subset analyses based on race, because race or ethnicity is not a biological categorization of populations. It's not scientific.

"Asian is a way of racial profiling," Brawley said. "The best way to scientifically profile is people who happen to have a receptor, which may very well be of a high prevalence in people who were born in Japan or China or maybe even Iraq. That's what we have to start doing."

"An Optimistic Presentation"

"This was, shall we say, an optimistic presentation," said Robert Temple, director of the FDA Office of Medical Policy, after hearing AstraZeneca's plans for further studies of Iressa. "The study, after all, failed. These are after-the-fact subset analyses in a study that didn't win. That's different than subset analyses in a study that did win.

"But what I really want to know is where you come out on the question of new patients with NSCLC being started on Iressa now. The materials you've put out say you should consider other drugs. Fine. Would it be your view that at the present time, optimism about the future data that might come forward notwithstanding, a person with this disease should not be started on Iressa?"

Responding for AstraZeneca, Mark Kris, chief of thoracic oncology at Memorial Sloan-Kettering Cancer Center, said "the most important thing is to put this into the context of what is available for a patient with advanced NSCLC, particularly after the failure of initial therapy."

"I think that the information that we have today is that there are some patients—those with an EGFR mutation—the literature to date says that they have an 89 percent chance of having a response," Kris continued. "As a clinician, my first point is to find those people that have that extraordinary chance to benefit, that is mutation-positive people, and the two surrogates for positive mutation we have today, that is never-smoking status from the US population, and worldwide, it's probably Asian."

TEMPLE: "You are looking at the mutation status of some people—200 you said—in the trial, and maybe that will be overwhelming. Do you have prospective data on that subgroup?"

KRIS: "The only prospective data that exists on the treatment of mutation-positive patients is, frankly, an extrapolation to the never-smoking patients. But these are placebo-controlled trials."

TEMPLE: "What I am really asking is what you really mean… One might say that you should use the drug that has very similar properties, similar mechanism, etc., that has shown an improved survival. Are you saying something to the contrary? I don't think it's clear yet. I sort of thought it was clear, but after this presentation, I don't."

KRIS: "I, frankly, think that the most incredible slide there was looking at the observations for the two subsets. I am putting my clinician hat on—it's not the AstraZeneca hat right now. There is effect here. You can argue the p value of .04 vs. .07, and there are people here who can do that much better than I. But from the clinician's standpoint, we have to make that choice. But you must remember, you also have a patient, you have a man with a squamous cancer sitting in your office that is smoking today. His likelihood of benefit, by the literature, is extraordinarily small—well under 5 percent.

"So for that patient, you are going to make another choice. The choice for that patient is not going to be decided by this trial."

TEMPLE: "I am really asking what your view *now* is on a person who is a candidate for an EGFR order of treatment, *now*, based on available data.

KRIS: "I am talking from a clinician's standpoint, and I interpret the whole of the data as unbelievably consistent. I think it's extraordinary that when you look at the mutations, when you look at the response rates across country, across drugs, it's how consistent it is, particularly the smoking observation."

TEMPLE: "The pattern may be the same. It may just be that this drug doesn't work as well as the other one, even though the pattern is the same."

KRIS: "Again, I can't rule out that possibility, but you can't look at any one piece of data, in my estimation, and this is one piece of data."

Richard Pazdur, director of the FDA Division of Oncology Drug Products: "You pointed out that you may

look at the mutational status in making the decision, but, really, in the US, only a small number of people really have that available."

KRIS: "From practice endpoint, I don't look at the mutation status. We can do that at our institution, but it's very limited availability right now. The decision is made on clinical grounds, and the surrogates for the mutation we have to date. And they are two: a never-smoking status and Asian birth. And that's how we make our decision."

Also speaking for AstraZeneca, Howard Burris, director of drug development for the Sarah Cannon Cancer Center in Nashville and an associate of Tennessee Oncology, said new patients in his practice are put on Tarceva rather than Iressa.

"Certainly the guidelines should be that those patients that were being treated on Iressa should be continued on Iressa," Burris said at ODAC.

"Those patients who fit into a class where it's felt appropriate that an EGFR inhibitor should be utilized that Tarceva, would, in fact, be the preferred agent… analyzing the data within our group, we have continued to accrue and randomize patients [on Iressa trials] of patients to a randomized phase III trial of patients with refractory lung cancer. We don't have a winner here, for many of us, the direction of this class is getting into what subsets will benefit, and for now we don't know direct head-to-head the differences between the two, Certainly, there are some small differences in terms of the mechanism of action, pharmacology and toxicity."

Switching To Tarceva

Lung cancer experts contacted by The Cancer Letter said they weren't putting new patients on Iressa. However, patients who appeared to have benefited from Iressa are staying on the drug.

"If they are benefiting from Iressa, if they are having tumor shrinkage or prolonged disease stabilization, I have no issues with keeping them on it," said Khuri. "If someone was responding and stopped responding, and it wasn't an explosive growth but a slow progression, what I am doing these days is switching them to Tarceva."

Explaining the rationale for switching these patients, Khuri said Iressa is approved at about a third of the maximum tolerated dose, while Tarceva is approved at MTD.

"Since it's closer to MTD, it may be possible to slow down the progression at that point," Khuri said. "The only use that I can see for Iressa is for someone who not tolerating Tarceva but benefiting from it, there I might consider switching to Iressa."

Khuri said he wouldn't put a patient on a hypothetical head-to-head trial of Iressa vs. Tarceva. "In patients with active disease where we have shown Tarceva has a survival benefit and Iressa doesn't, I would not be comfortable starting a patient on it," he said.

However, a trial of Iressa vs. no treatment in advanced disease would be ethical since there is no proof that Iressa prolongs survival. "In fact, I have no issues in enrolling people in an adjuvant therapy trial, because that's earlier stage, where many agents are more active than in advanced disease settings," he said. "They are getting surgery followed by chemotherapy, and then they are randomized to Iressa or no Iressa. I am putting patients on that trial."

Albain said she places new patients exclusively on Tarceva, but continues to renew Iressa prescriptions in patients who are benefiting from the drug who have already started it.

"I define benefit as shrinkage of tumor or prolonged stable disease," Albain said. "I have patients who are continuing in their second and third year of survival on this agent with rock-stable disease and excellent performance status. Added to this, of course, would be a favorable toxicity profile. If a patient is experiencing significant toxicity and isn't responding, you wouldn't continue it. I think it's important to continue it to maintain a prolonged stable disease status as it is as important to maintain a remission status."

Albain said there is no data on switching from one TKI drug to another.

"Right now there is nothing to support switching from one to another in either direction," she said. "It would be intriguing to look at some Iressa non-responders and determine whether there would be subsets that would respond to Tarceva and vice versa. That is a very important question, and that is a trial that very much needs to be considered."

Albain said it would be ethical to compare bioequivalent doses of Iressa and Tarceva. "A trial comparing bioequivalent doses of the two agents would be very attractive," she said. "One could name a number of other studies that would also be ethical to have an Iressa arm in, if you are selecting patients who are at high likelihood to respond, because we clearly know that there is a subset of patients who respond dramatically to both of these agents.

"That's really where the challenge is in 2005, to get the trials done in this group of patients and sort out whether these drugs indeed are identical in this group of patients, or whether there are differences where one

could predict who might respond to one versus the other, or both," Albain said.

Ruckdeschel said he, too, is prescribing Iressa to patients who have benefited from it, but placing new patients on Tarceva.

"We, as an institution, are switching to Tarceva, based on the letters we are getting from the company, that there is no clear improvement in survival," Ruckdeschel said. "But, on the other hand, there are clearly patients who have received Iressa who have done spectacularly. I still have one who is five or six years out with bone mets on Iressa."

Ruchdeschel said he would have ethical problems with doing a hypothetical study of Iressa versus chemotherapy in advanced disease.

"If it's an advanced disease study of Iressa versus chemo, it would probably be like using cisplatin alone, but if it's adding Iressa or not adding Iressa after a bunch of other treatment, I don't really have a problem with that," he said. "Clearly, some of the data on Iressa suggest that it was more effective in cells that have previously seen chemotherapy than in cells that have not. So, an adjuvant study that does whatever you are going to do and then does Iressa afterwards or not, I am still okay with that."

Lung cancer experts said it would be unnecessary for FDA to pull Iressa off the market.

"It would be incredibly stupid for ODAC to pull that drug, or to recommend pulling that drug, or for FDA to pull the drug," said Ruckdeschel. "People are using it, people are benefiting from it, let them use it for God's sake. The marketplace will handle its utilization."

Funding Opportunities:

RFP Available

RFP N02-CO-51018-17: Development of a Common Biospecimen Coordination System and Informatics Infrastructure for NCI Prostate Specialized Programs of Research Excellence

Response Due Date: May 4

NCI seeks a contractor to develop a design plan and budget for system implementation of a common biospecimen coordination system and informatics infrastructure for multiple NCI Specialized Programs of Research Excellence in prostate cancer research. The system shall facilitate biospecimen and data sharing among scientific investigators located at different institutions through standardized approaches of collecting, processing, storing, annotating and distributing high-quality biospecimens. Initially, the system shall support the Inter-SPORE Prostate Biomarkers Study, a validation study of prospective prostate cancer biomarkers. Ultimately, the purpose of the project is to serve as a pilot for the evolving National Biospecimen Network by developing an infrastructure to annotate and integrate specimen banks, such as those of the SPOREs, to enhance the quality and availability of various biospecimens and associated data for the broader scientific community. The major components of the BCS include: (1) Human subjects protection, privacy protection and informed consent processes; (2) Rigorous standard operating procedures for biospecimen collection, processing, annotation, storage and dissemination; (3) Quality assurance/ quality control; (4) Integration with associated clinical data, both retrospectively and prospectively; (5) Informatics system requirements; (6) Biospecimen and data access policies; (7) Biohazard considerations and packing, shipping and storage policies; (8) Intellectual property/Ongoing system oversight and maintenance; (9) Establishment of a common repository for biospecimens unused by the IPBS; and (10) Personnel management.

The RFP is available at http://www.fbodaily.com/archive/2005/03-March/19-Mar-2005/FBO-00770630.htm.

In Brief:

Antonio Scarpa To Direct Center For Scientific Review

(Continued from page 1)

Relations group, based in Washington, D.C. Mack retired in 2001 after serving 18 years in Congress, and joined the law firm of Shaw Pittman. **President Bush** recently appointed Mack to lead a bipartisan Advisory Panel on Federal Tax Reform. Coats retired in 1999 after serving 10 years in the Senate and eight years in the House. In 2001, President Bush named Coats ambassador to Germany, where he served through March 3. Mack brings five other government relations specialists from Shaw Pittman: **Tom Spulak, Andrew Woods, Mark Smith, Viraj Mirani**, and **Claudia Hrvatin**. . . . **ANTONIO SCARPA** was appointed director of the NIH Center for Scientific Review, effective July 1. Scarpa is the David and Inez Myers professor and chairman of the Department of Physiology and Biophysics at Case Western Reserve University. He will replace **Brent Stanfield**, who became acting director of CSR since October 2003, following the departure of **Ellie Ehrenfeld**. . . . **DOUGLAS BLAYNEY** was named editor of the American Society of Clinical Oncology's new Journal of Oncology Practice. Blayney is medical director at the University of Michigan Comprehensive Cancer Center and clinical professor of medicine at the University of Michigan. . . . **FRANCINE FOSS** was appointed professor of medical oncology at Yale Cancer Center, said center director **Richard Edelson**. Foss is director of the Lymphoma and Experimental

Therapeutics Group at Tufts New England Medical Center. She designed and directed multi-center clinical trials of two pharmacologic agents for lymphoma that were approved by FDA. One of these, Interleukin-2 conjugated to Diphtheria toxin, was the first FDA approved fusion biologic drug to be approved in the U.S. With the introduction of intravenous infusions of autologous immature dendritic cells before an allogeneic bone marrow transplant, Foss reduced the development of graft-versus-host disease in patients from the average of 40-50 percent to 15 percent. These findings were confirmed in a national phase II trial. For this advance, Foss received the George Santos Award from the American Society of Bone Marrow Transplantation last year. . . . **OHIO STATE UNIVERSITY** Comprehensive Cancer Center received a $1.8 million grant from NCI to study how the immune system responds to basal cell carcinoma. **Ronald Glaser**, professor of molecular virology, immunology and medical genetics, will lead the study of 320 patients who have undergone surgery to remove BCC tumors. . . . **HHS SECRETARY MIKE LEAVITT** named six people to his senior staff. **Rich McKeown** will serve as chief of staff. He was Leavitt's chief of staff at the Environmental Protection Agency and the Utah Governor's Office. **Kerry Weems** was appointed deputy chief of staff. Weems, a 21-year veteran of HHS, most recently served as acting assistant secretary for budget, technology and finance. **Jennifer Young** was named acting senior counselor for health policy, a new position. Prior to this appointment, Young was appointed by President Bush and confirmed by the Senate to serve as assistant secretary for legislation. She will continue in this role until a replacement is named. **William Raub** was appointed acting counselor for science policy, overseeing issues involving FDA, NIH, and CDC. He also will serve as an advisor on counterterrorism. Raub was principal deputy assistant secretary for public health emergency preparedness and previously served as acting assistant secretary for planning and evaluation. **Richard Campanelli** will serve as acting counselor for human service policy. He will continue as director of the Office for Civil Rights. **Natalie Gochnour** will serve as counselor to the Secretary on communication and policy. She has worked in numerous roles with Leavitt since 1993. . . . **SUSAN ARBUCK** was appointed vice president, oncology, global clinical development, for the Schering-Plough Research Institute. Arbuck was vice president and global head of the oncology therapeutic area at Aventis Pharmaceuticals.

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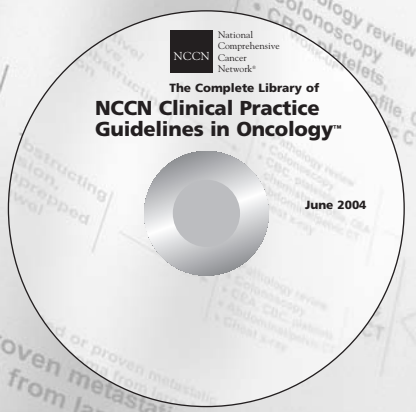

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