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FDA Advisors Recommend Approval Of Taxol For Node-Positive Breast Cancer

The FDA Oncologic Drugs Advisory Committee last week recommended approval for Taxol (paclitaxel) Injection for sequential administration to doxorubicin-containing therapy for the adjuvant treatment of node-positive breast cancer.

In another action at its meeting Sept. 16-17, the committee recommended approval for UFT capsules in combination with leucovorin calcium tablets for the first-line treatment of metastatic colorectal cancer. Both the Taxol and UFT-leucovorin therapies are sponsored by Bristol-Myers Squibb Co.

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In Brief:

Justice Department Files Civil Suit To Recover $25 Billion From Tobacco

LOVE AND HATE in the tobacco war: Tobacco marketing, which has never been particularly tasteful or truthful, took a strangely prescient turn last week with Brown & Williamson Tobacco Corp.'s "we love you" advertising campaign.

The campaign invites calls to the company's toll-free phone number, 800-578-7453. After persons under age 21 and nonsmokers are advised to hang up, a recorded, saccharine male voice tells callers, "We, the Brown & Williamson Tobacco Corp., are in love with you. Yep, you heard right. Brown & Williamson Tobacco is in love. We're a giant corporation and you make us feel like a little kitten! Thank you, lover. By the way the other tobacco companies hate you and think you're ugly. They told us so. Now, press 1 to be put on our mailing list. Press 2 to find a store near you. Press 3 to speak with a customer service representative."

As Brown & Williamson began declaring its love of the increasingly socially unacceptable and unenviable American smoker, the U.S. Justice Department demonstrated its disdain for the tobacco industry's successful wooing of smokers for the past half-century.

With a snarling accusation that the industry has conducted a "coordinated campaign of fraud and deceit," the Justice Department filed suit against U.S. tobacco companies on Sept. 22 to recover billions spent by federal civilian and military health insurance programs on smoking-related illnesses. These expenses were not covered by the $246 billion settlement the industry reached with the states last year.

The suit, filed in U.S. District Court in Washington, DC, alleges the

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ODAC Recommends Against Evacet And Roferon-A

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The committee recommended against approval for:

—Roferon-A (interferon-alpha 2a) as adjuvant therapy for malignant melanoma. The application, presented by sponsor Hoffmann-La Roche, was marred by the absence of the complete data set. The poor quality of the company's presentation led two members of the committee to sharply criticize Roche and FDA for bringing the application to ODAC.

—Evacet (liposomal doxorubicin) for the first-line treatment of metastatic breast cancer in combination with cyclophosphamide. The drug is sponsored by The Liposome Co.

FDA Presents Subset Analysis

Voting for approval of Taxol, ODAC disregarded the FDA staff contention that the data did not support approval for estrogen receptor-positive and progesterone receptor-positive patients.

The agency's skepticism was based on the analysis of a very large subset of data—about two-thirds of the total 3,121 patients involved in the intergroup trial led by Cancer and Leukemia Group B, the study that formed the foundation of the BMS application.

Though not prospectively defined and not statistically significant, the subset analysis data demonstrated no overall survival advantage and no disease-free survival advantage for women whose tumors were ER-positive and PR-positive, and who received tamoxifen. Women who fit into this category should be followed until the impact of the therapy becomes measurable, FDA recommended.

The agency recommended that the Taxol-doxorubicin regimen be approved for ER-negative and PR-negative patients.

Basing a recommendation on a subset analysis is an unusual position for FDA, agency officials acknowledged. However, the ER+/PR+ subset in this case was unusually large: 2,066 patients, two-thirds of the total enrollment, said Robert Temple, associate director for medical policy at the Office of Drug Evaluation I of the FDA Center for Drug Evaluation and Research.

"We are usually on the other side of this argument," Temple said at the ODAC meeting. "We are historically skeptical about subgroup analysis. I think the theme here is that this sort of grabs you by the hair more than most of them do. It's just that when you see two-thirds of the study with the hazard ratio of approximately one, you sort of have to say, what shall I do with it? I would consider this quite exceptional."

Overall, patients who received Taxol and doxorubicin had a 22 percent decrease in risk of relapse and a 3.6 percent increase in three-year disease-free survival. (The hazard ratio was 0.78).

After the investigators—and subsequently FDA—performed an analysis of the overall survival and disease-free survival data, they found that receptor negative patients who received Taxol and doxorubicin had a 34 percent decrease in risk of relapse, and a 10.5 percent difference in three-year disease-free survival. (The hazard ratio was 0.66).

By contrast, receptor-positive patients showed no difference in disease-free survival. In accordance with the protocol, nearly all receptor-positive women received tamoxifen after completing chemotherapy.

"If a woman is having chemotherapy, and is going through the tail of it, if they are on tamoxifen, you want to be sure that you are giving them something back for adding Taxol," said ODAC member Derek Raghavan, head of medical oncology at the University of Southern California Norris Comprehensive Cancer Center. "I think this is one of the more difficult decisions we've had to make."

CALGB investigators disagreed.

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"There are a very good kinetic reasons for why these effects are so," said Larry Norton, chairman of the CALGB Breast Committee and a physician at Memorial Sloan-Kettering Cancer Center. "ER-positive disease grows more slowly. The effect of chemotherapy may be less because it's growing more slowly, as is universally seen in all models we've looked at, but also it takes longer to see a benefit, because it takes longer for patients to relapse."

Norton said excluding ER-positive women from the indication could deny them a chance to benefit from the therapy. "Let's say we decided not to give Taxol to ER-positive patients," Norton said. "Let's say five years from now we find out that the curves start to separate once we get through three-and-a-half years, then we cost a lot of women their lives.

"If we decide, however, to give Taxol, and it turns out, in the long term, not to be effective, what have we really cost them? We caused some toxicity, but compared to what they've received with AC, and compared with many other things we do in oncology, it's really very minimal," Norton said to the committee.

ODAC member Kim Margolin agreed.

"We have to consider that the addition of Taxol is going to have an impact on all groups similar to the addition of chemotherapy to hormonal therapy for patients for ER-positive disease," Margolin said.

Before making a treatment decision, clinicians consider a patient's menopausal and estrogen receptor status, as well as the level of estrogen and progestron receptors, Margolin said. "[The National Surgical Adjuvant Breast and Bowel Project] has tried in some of their retrospective analyses to look at the outcomes in various studies as grouped by the level of ER- and PR-positivity," Margolin said. "They've taken a stance in many of their studies prospectively that they don't care. They just put everybody over 50 on tamoxifen. So I think that rather than try to say that this is Group A and Group B, we have to remember that we have quite a spectrum, and it makes more biological sense to look at it that way."

Margolin suggested giving Taxol the indication. However, the agency could note prominently on the label that the benefit of the Taxol-doxorubicin combination is not proven for ER-positive patients. Thus, a note inserted in the "indications" section of the label could flag a passage contained in the "clinical trials" section.

"It seems to me that we ought to accept the overall results of this large, powerful trial," agreed ODAC member David Johnson, director of the Vanderbilt University Medical School Division of Medical Oncology. "I like the idea that we put the data into the package insert."

The susbset analysis is clearly relevant to clinical decisions, Johnson said. "I am not sure how I am going to handle a patient with positive nodes who is ER and PR-positive," he said. "Candidly, I've been going toward using the sequential therapy, and now that I see these data, I am a bit hesitant about it."

Disclosure of the data would be appropriate, said patient representative Sandra Zook-Fischler. "As a patient representative, I have to take the patient position, and that is that patients need the options," Zook-Fischler said. "I would like to be able to sit down with my doctor and decide what's best for me."

The committee voted unanimously to approve Taxol for the indication. Before the vote, ODAC member Raghavan said he was convinced by the argument that withholding the drug would cause more damage than approval. "Until we have data, we should be conservative in favor of the patient," Raghavan said. "I was the person who raised the questions, but I am pretty comfortable that my questions have been resolved."

The CALGB-led intergroup trial was the largest adjuvant breast cancer study ever conducted.

"In a challenging disease like cancer, where ground-breaking advances are often made in only minor increments, this recommendation represents a major step forward for patients," Richard Schilsky, associate dean for clinical research, University of Chicago, and chairman of CALGB, said in a statement. "It is even more critical now that women with breast cancer are diagnosed and treated early to increase their chances of living disease free."

Schilsky, who is also the chairman of ODAC, did not take part in either the voting or the discussion of the application.

"[ODAC's] recommendation further supports the clinical benefit of Taxol," said Renzo Canetta, BMS vice president, clinical oncology. "This study which demonstrates Taxol improving survival in patients with early stage breast cancer illustrates why we remain committed to researching new applications and developing Taxol to its fullest potential."

Of the more than 180,000 women diagnosed with breast cancer each year in the U.S., approximately 40 percent are candidates for adjuvant therapy.

Taxol is approved as first-line (in combination with cisplatin) and subsequent therapy for the

treatment of advanced cancer of the ovary and for the treatment of breast cancer, after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy. Prior therapy should have included an anthracycline, unless clinically contraindicated.

The drug is also indicated for use in combination with cisplatin for first-line treatment of non-small cell lung cancer in patients who are not candidates for potentially curative surgery and/or radiation therapy, and for second-line treatment of AIDS-related Kaposi's sarcoma.

Taxol side effects include myelosuppression, hair loss, peripheral neuropathy, myalgia/arthralgia, diarrhea and nausea. A less frequent but serious side effect is severe hypersensitivity reaction, which is demonstrated by symptoms of shortness in breath, low blood pressure and rash. Patients who receive Taxol should be premedicated to prevent this reaction.

UFT-LK Not An "Important Advance," But Is Approvable, Committee Finds

ODAC unanimously concluded that UFT (uracil and tegafur) capsules in combination with leucovorin calcium tablets provides equivalent survival compared to the current IV standard therapy for the first-line treatment of metastatic colorectal cancer.

Though the committee unanimously recommended approval, the FDA's decision is likely to be determined by the agency's interpretation of "fixed combination" regulations, which require that all components of a drug contribute to its safety and efficacy.

The agency said it recently informed BMS that the New Drug Application did not demonstrate that uracil contributed to the fixed combination. BMS has since submitted data on the combination of uracil, but the agency's review of these materials is not yet complete. The "fixed combination" requirement can be waived for "important therapeutic advances." However, the committee decided that UFT/LK is not an important therapeutic advance.

The company's application was based primarily on the results from two randomized phase III, multi-center clinical trials comparing oral UFT plus leucovorin calcium to intravenous 5-fluorouracil plus leucovorin. The BMS-011 and the BMS-012 studies were designed to compare the combination of UFT capsules plus leucovorin calcium tablets to IV 5-FU plus IV leucovorin in patients with metastatic colorectal cancer.

The BMS-011 study is the largest registrational phase III clinical trial ever conducted in advanced colorectal cancer. Combined with the BMS-012 study, the two trials enrolled nearly 1,200 colorectal cancer patients. The results from these trials demonstrate that the median survival time for the combination of UFT plus leucovorin is similar to the current the current standard therapy of IV 5-FU and leucovorin (12.4 months vs. 12.6 months), the company said.

However, the FDA statistical analysis of study 11 showed that survival on the UFT/LV arm could have had as much as a 20 percent lower survival than the FU/LV arm. According to the worst-case scenario envisioned by the agency, as much as 2.68 months could have been lost on the UFT arm.

Seeking ODAC's advice on the meaning of this potential drop in survival, the agency asked the committee how much of the survival effect of the control regimen would the committee be willing to lose with the UFT/LV regimen and still call the UFT/LV regimen equivalent to the control regimen.

Though no vote was taken, committee members said a potential 20 percent loss would be acceptable.

"The reality is that these two curves are so precisely the same that it seems to be that it's a lot of effort for not a clinically relevant issue," said committee member Johnson.

"One looks at the survival curves, as my distinguished Southern colleague pointed out, they are very similar," said Raghavan, agreeing with Johnson's observation. "I think I would really like to have heard FDA concentrate more on what I think is the fundamental issue: There is an orally-administered drug which has been designed to reduce the problems of having chemotherapy. To me, it's a no-brainer. Patients like to take things by mouth rather get stuck with a needle, and to take them at home rather than to come to a clinic. So I don't have a lot of interest in comparing 52 versus 53, versus 51 weeks. But I would be very interested in your sense of the issues that we raised related to toxicity. Does it make toxicity less?

"The thing I am really interested in knowing about this product is what is the patient benefit from the perception of FDA? Is it easier to take? Do they live better lives?"

Responding to Raghavan's question, FDA medical reviewer Robert White said the sponsor's quality of life assessment showed no difference between the two arms. "The reduction of toxicity that is being claimed didn't seem to result in any improvement in the quality of life," White said at the

meeting.

The company confirmed that attempts to assess the patients' quality of life detected no difference between the two arms.

However, the value of an oral therapy could have been obscured in this patient population, said committee member Margolin. "In this study patients had a very short duration of treatment," Margolin said. "The value of a quality of life analysis when patients are falling off as quickly as they are has to be quite limited. The quality of life and the impact of an oral therapy versus a relatively nontoxic IV chemotherapy are probably much more useful in a patient group that is being treated longer, or if it's adjuvant."

In the individual studies UFT plus leucovorin was associated with significantly fewer side effects, such as myelosuppression, including infections, as well as significantly fewer non-hematological toxicities, such as stomatitis and mucositis, compared to IV 5-FU and leucovorin, the company said. Also, the patients treated with the oral regimen demonstrated a reduced need for supportive therapy and concomitant medications, including antiemetics, antibiotics, and growth factors.

However, toxicity profiles of the two therapies may not be easily gauged in the quality of life surveys, said committee chairman Schilsky. "One might argue that the reduction in mucositis on the UFT arm was balanced by an increase in by the increase in diarrhea," Schilsky said. "Some of the other toxicity reduction, which the physician may appreciate as being potentially important may be unrecognizable by the patient."

To approve the therapy, FDA would have to decide whether uracil and tegafur—the components of UFT—can be combined into the same capsule. Regulations preclude the agency from approving "fixed combinations" of drugs unless each component of the combination contributes to the safety or efficacy of the therapy. However, the agency could consider a waiver from the fixed combinations regulation if the committee decides that UFT represents an important therapeutic advance in the therapy of metastatic colorectal cancer.

Recently, Bristol submitted additional data on the contribution of uracil to the combination. These data are still being considered by the agency.

If the agency is convinced that uracil makes a contribution to the therapy, UFT should be approved, ODAC recommended in an 11-0 vote.

However, the committee said the UFT/LV regimen does not represent an important therapeutic advance in the treatment of advanced metastatic colorectal cancer. "This is not a therapeutic development," said James Krook, former ODAC member who returned as a voting consultant on the UFT application.

In an 8-0 vote with three abstentions, the committee decided that the therapy should not qualify for a waiver.

Roche Application Marred By Missing Data Set

In a 7-0 vote with two abstentions, the committee shot down the Hoffmann-LaRoche supplemental New Drug Application for Roferon A (interferon-alpha2a) as an adjuvant therapy for malignant melanoma.

In the course of questioning by the committee, Roche officials acknowledged that:

1. The data set from the pivotal trial—Study M 23031, "Adjuvant Therapy Following Wide Excision of Poor Prognosis Stage I Malignant Melanoma (Breslow thickness >1.5 mm)" did not exist, and therefore could not be audited.

2. The protocol could not be located, either.

3. The data in the sNDA were not updated since the application was filed with FDA in 1997.

4. Protocol compliance in the pivotal study, which enrolled 498 patients in 32 centers in France, was not uniform.

5. There was no central review of pathology slides.

6. Data on several patients on both arms of the pivotal study had been lost.

Moreover, the endpoint of the French study—disease free interval—was of uncertain value to patients. But even the company's claim of an increased DFI was not statistically significant after adjustments for Breslow thickness and gender.

A confirmatory study conducted in Austria did not prospectively specify the endpoints and did not include a statistical plan in the protocol. Even the FDA attempt at a meta-analysis, which included the data on Schering-Plough's interferon, showed some improvement trends on the interferon arm, but did not reach statistical significance.

After being confronted with this parade of evidence, ODAC member Johnson said he was dismayed by the presentation. Another committee member, Raghavan, said he could not fathom why so weak an application was presented to the committee in the first place.

"I think the overall data are highly questionable,"

Johnson said. "These are not the quality of data that we see come to this agency that generate approval by this body."

The problems begin with the endpoint of the French study, Johnson said. "Disease-free interval, in the absence of a survival benefit, is an uncertain benefit, in my view. If they had shown some meaningful patient benefit, perhaps I could have accepted it as an endpoint of value, but I haven't seen these data.

"I find it shocking—and I think that's the word—that a study of this size would be undertaken without appropriate stratification for known prognostic endpoints," Johnson said. "That being said, even more importantly, there was no quality control of the follow-up. There was no central review of the patient pathology. [Patients] could have been one stage in the Roferon arm and quite another on the other."

Raghavan said FDA should not have brought the application to ODAC.

"I always feel sorry for FDA, because they are victims, and they get beaten up by everyone," Raghavan said, addressing the FDA staff at the meeting. "But as a taxpayer, I really have to say that I don't think you've done as well as you usually do. You've left it to the committee to identify a whole series of very bad statistical concepts and poor quality data. I shouldn't have to remind you: Garbage in/garbage out, no matter what the p-value. I feel very disappointed that we had to go through this exercise."

Turning to the FDA meta-analysis, Raghavan said he objected to pooling the Roferon data with those of Schering's Intron. "Bending over backwards, bringing in Intron data that were approved based on good-quality data, and then tainting that information with poor-quality information sets a precedent that is kind of disappointing," he said.

"I apologize for beating you up, but you deserve it," Raghavan concluded.

Raghavan's comments echo the frustration that is frequently expressed by FDA insiders and advisors. The recommendation of an advisory committee has historically been the agency's preferred defense against political retribution from unsuccessful sponsors and Congressional critics. However, throwing badly prepared applications to advisory committees has a cost. In recent years, members of advisory committees have been asking the FDA staff to do a more thorough job of filtering out applications that clearly lack the data to support approval.

Jay Siegel, director of the Office of Therapeutics Research and Review of the FDA Center for Biologics Evaluation and Research, said the agency's review of the Roche application was thorough.

"I don't think there was a flaw discussed here that was not identified by FDA," he said.

"As to the question as to why these data were brought before the committee, perhaps this requires a bit of an understanding of the time lines," Siegel said. "At the time we need to make a decision of going to schedule the committee, it's usually a couple of months before the committee. As we have made clear in the presentation, we felt that based on the [French] study alone, we felt that there was no reason to consider the approval of this application. What we had available to us two months before this committee was a published report of the [Austrian] study that showed a p-value of .02, and no information from the company that they weren't going to be able to get the data set and the protocol. Within the past week or two, we have seen a preliminary analysis, the study did not look like what we expected it to look like."

In the US, Roferon-A is approved for chronic myelogenous leukemia, hairy cell leukemia, AIDS-related Kaposi's sarcoma, and hepatitis C. The agent is approved for stage II malignant melanoma in 16 countries, including the European Union.

ODAC Votes Down Liposomal Doxorubicin

The committee recommended against approval of a New Drug Application for Evacet (doxorubicin HCl liposome injection) for the first-line treatment of metastatic breast cancer in combination with cyclophosphamide. The drug is sponsored by The Liposome Co. Inc.

The application was based on two completed studies designed to measure cardiotoxicity and tumor response rate. Generally, FDA does not accept response rate as a basis for full approval of drugs. However, in the case of Evacet, response rate could be viewed as a surrogate for patient benefit, said Grant Williams, a medical officer in the oncology division of the FDA Center for Drug Evaluation and Research.

"[Evacet], a liposomal doxorubicin, is a special case," Williams said at the meeting. "It has the same active moiety as doxorubicin. We were doing something different in using response rate for first-line approval. Because we have the same drug, same molecule, and we are using it as a surrogate of what we think that effect is going to have on ultimate survival years down the line."

At a meeting five years ago, the agency and the company agreed that trials designed to demonstrate Evacet's non-inferiority to doxorubicin would be conducted. One of the studies demonstrated a significantly lower cardiotoxicity in the Evacet/cyclophosphamide arm. However, response rates were much lower than anticipated in both arms, and the studies ended up underpowered to detect antitumor efficacy, the agency said.

A second study showed identical response rates of 26 percent for both the Evacet and doxorubicin arms. Overall median survival was 14.6 months in the Evacet arm and 20.1 months in the doxorubicin arm. The findings were not statistically significant.

"[Originally] we were interested in how much of the antitumor or beneficial effect imparted by doxorubicin we are losing, and I don't believe we would ever conceived of using response rate in the 20s range to demonstrate equivalence for that effect," Williams said. "The response rate was lower than planned, the study was underpowered for the outcome and we don't have a study showing equivalence that we wanted."

Raghavan agreed. "I don't think we are being bureaucrats and being persnickety about trials," he said. "I think we are actually asking, Is there evidence that to cut down toxicity (which can be avoided in other ways) we are not sacrificing cure rates or response rates?"

"I think we have the problem of not enough information."

The committee voted 9-2 against approval.

NCI Programs:

Funding To Help Establish DNA Microarray Facicilities

NCI has selected 24 cancer research centers to receive $4.1 million to purchase equipment needed to establish DNA microarray facilities.

DNA microarray technology is a new research tool that allows scientists to assess the level of expression of a large subset of the 100,000 human genes in a cell or tissue. The facilities will offer technological support to scientists who study the molecular causes of cancer. By awarding the funding, NCI expects that the new technology will be more widely available to cancer researchers and that it is applied to a broad spectrum of problems in cancer research.

"This technology can quickly produce a snapshot of the genes that are active in a tumor cell, critical information in narrowing down the precise molecular causes of a cancer," said NCI Director Richard Klausner. "It is absolutely imperative that cancer researchers have open access to this technology, and the NCI-supported facilities help to ensure that this is the case."

Klausner said the microarray centers also will support the work of scientists involved in a new NCI initiative titled, "The Director's Challenge: Toward a Molecular Classification of Tumors." The five-year initiative aims for the first time to define tumor cells based on their unique molecular changes, information that promises to improve the diagnosis and treatment of cancer.

The sites of the 24 DNA microarray facilities are: Arizona Cancer Center, Tucson, AZ; The Burnham Institute, La Jolla, CA; Case Western Reserve University, Cleveland; Dana-Farber Cancer Institute, Boston; Fox Chase Cancer Center, Philadelphia; H. Lee Moffitt Cancer Center, Tampa, FL; Lineberger Comprehensive Cancer Center, Chapel Hill, NC; Massachusetts Institute of Technology Center for Cancer Research, Cambridge, MA; Mayo Clinic Cancer Center, Rochester, MN; M.D. Anderson Cancer Center, Houston; Ohio State University, Columbus; The Scripps Research Institute, La Jolla; St. Jude Children's Research Hospital, Memphis, TN; University of California, Irvine; University of California, San Francisco; University of Chicago Cancer Research Center; University of Colorado Health Science Center, Denver; University of Nebraska Medical Center, Omaha; University of Pennsylvania, Philadelphia; University of Pittsburgh Cancer Institute; University of Texas, Medicine Branch, Galveston; University of Virginia Cancer Center, Charlottesville, VA; Vanderbilt Cancer Center, Nashville; and Yale Cancer Center, New Haven, CT.

In Brief:

Justice Sues Tobacco Industry For Cost Of Cigarette Smoking

(Continued from page 1)

cigarette companies conspired since the 1950s to defraud and mislead the American public and to conceal information about the effects of smoking. In filing the civil suit, the department closed its criminal investigation of the industry. "Smoking is the nation's largest preventable cause of death and disease, and American taxpayers should not have to bear the

responsibility for the staggering costs," Attorney General **Janet Reno** said. "For more than 45 years, the cigarette companies conducted their business without regard to the truth, the law, or the health of the American people."

In addition to monetary damages exceeding $20 billion a year, the suit seeks to require the industry to fund education programs about the health effects of smoking.

The suit names Philip Morris Inc., R.J. Reynolds Tobacco Co., American Tobacco Co., Brown & Williamson Tobacco Co. Inc., British-American Tobacco PLC, Lorillard Tobacco Co., the Liggett Group, the Council for Tobacco Research U.S.A. Inc., and the Tobacco Institute Inc.

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JOHN DURANT, executive vice president of the American Society of Clinical Oncology, has been named consulting medical director of Walther Cancer Institute, in Indianapolis. Over the past 14 years, the institute has contributed more than $33 million to collaborative cancer research projects at Indiana University, Purdue, Notre Dame, Michigan and other Midwest universities and medical centers. Durant said the his duties at Walther will be to further those collaborations. **Jim Ruckle**, executive vice president of the institute, said Durant's national reputation "will help medical, health care and government officials, as well as the general public, understand and support the important work of the Institute to find cancer cures through basic, clinical and patient-care research." . . . **PRESIDENT CLINTON** proclaimed the week of Sept. 19-25, "Ovarian Cancer Awareness Week." According to the proclamation, "Our most effective weapon in the battle against ovarian cancer is early detection. Subtle but recognizable symptoms, such as bloating, vague abdominal pain and discomfort, gastrointestinal problems, back pain, and fatigue can also be symptoms of other less serious illnesses, but women who are experiencing such early warning signs should consult their doctors immediately for appropriate tests." . . . **SMITHKLINE BEECHAM** invites abstract submissions from oncology fellows for presentation at the Fourth Annual Oncology Fellows Forums. The deadline for gynecologic oncology submission is Dec. 3; the forum is scheduled for Feb. 24-27. For medical oncology, the deadline is Dec. 10; the forum is scheduled for March 2-5. Contact Una Kistner or Peggy Protopapadakis of STI at 973-376-5655. . . **DORIS DUKE** Charitable Foundation announced research award winners for the Doris Duke Clinical Scientist Award Program. The award brings $100,000 per year for three years to physician-scientists. The six awardees are: **Lisa Carey**, UNC-Chapel Hill School of Medicine; **Theodore DeWeese**, Johns Hopkins Oncology Center; **James Ford**, Stanford University School of Medicine; **Nancy Keating**, Harvard Medical School; **Mathew Smith**, Massachusetts General Hospital; **Robert Vonderheide**, Dana-Farber Cancer Institute. . . . **MARK CORNFELD** was appointed medical director for the Fox Chase Cancer Center CanPrevent corporate services program and associate medical director for the Fox Chase Network of community hospitals. He will work with **Paul Engstrom**, FCN medical director and senior vice president of population science. Cornfield was medical director of the cancer program at St. Francis Medical Center in Trenton, NJ. . . . **ROBERT F. WOLFE** and Edgar T. Wolfe Foundation announced a $6.5 million contribution to the Arthur G. James Cancer Hospital at Ohio State University. The contribution will benefit the Human Cancer Genetics Program in research and scholarship. The program is led by **Albert de la Chapelle**. . . **RICHARD BORNSTEIN**, 60, of Cleveland, OH, died of an apparent heart attack on Aug. 18. He was director of the Mount Sinai Medical Center Oncology Treatment Program, Center for Breast Health and a founding editor of Seminars in Oncology. . . **MONICA MORROW** was named director of the Cancer Department of the American College of Surgeons. Morrow is professor of surgery at Northwestern University School of Medicine, and director of the Lynn Sage Comprehensive Breast Program at the Northwestern University Memorial Hospital. . . **CANCER RESEARCH FOUNDATION** of America Congressional Families Program honored **Katie Couric**, co-anchor of the NBC show "Today;" **Debbie Dingell**; and **Richard Hirsh**, chief of diagnostic radiology at Akron City Hospital. . . . **SAVE TIME** searching the massive and remarkably convoluted mishmash of NCI web pages. The **Association of Cancer Online Resources** provides a free service, "Search the NCI Servers," at http://educate.acor.org/ncisearch/. Amazingly enough, NCI's own web pages do not offer a search function for the Institute's entire site. At the ACOR site, the full-text search performed well on nonscientific tests by **The Cancer Letter** editors. Its ease of use stands in sharp contrast to the hunting and clicking we've had to do in the past on the NCI website.

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