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FDA Requires Independent Confirmation Of Disease Progression In Group Trials

By Paul Goldberg

The results of a cooperative group trial of Avastin with chemotherapy in first-line metastatic breast cancer received a standing ovation at the 2005 annual meeting of the American Society of Clinical Oncology.

The results were spectacular: progression-free survival increased from six months to 11 months in patients getting Avastin (bevacizumab), and the p-value was solid, less than .001.

However, on Sept. 11, FDA bounced these results back to Genentech with a demand for additional documentation. The agency asked to see an independent review of scans that would document progression-free survival, the study's primary endpoint.

"It was a bit of a surprise," said Kathy Miller, the principal investigator of the trial conducted by Eastern Cooperative Oncology Group and a breast cancer expert at the University of Indiana School of Medicine.

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NCI Programs:

Cancer Center Directors Call For Collaboration, Funding, Broad Application Of Best Practices

By Kirsten Boyd Goldberg

The directors of the NCI-designated cancer centers said the cancer mortality rate could be reduced by broader application of methods of early detection, prevention, and treatment that are available now.

The 61 NCI-designated cancer centers should collaborate in research and dissemination of best practices, and should advocate "aggressively" for increased public awareness and governmental funding for cancer research, according to a report the directors presented to the National Cancer Advisory Board Sept. 7.

The report was developed in response to the previous NCI director's goal to "eliminate the suffering and death due to cancer by 2015." Cancer center directors revolted against the widely-criticized goal in a meeting with former director Andrew von Eschenbach last fall. The center directors formed a committee to come up with realistic ways that cancer centers could accelerate the reduction of cancer incidence and mortality (The Cancer Letter, Nov. 23, 2005).

M.D. Anderson Cancer Center President John Mendelsohn, who led the center directors committee, made it clear that the directors didn't share von

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FDA Seeks Documentation On Avastin In Breast Cancer

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In the past, FDA accepted that peer review and auditing procedures used by the groups conveyed validity on their data. While companies were expected to set up central review of patients' scans, the agency was willing to accept the investigators' judgment in data submitted by the groups. Now, the agency has decided that the same standard should apply to everyone.

Richard Pazdur, director of the FDA Center for Oncology Drug Products, declined to discuss the Avastin application, citing agency regulations that make such matters confidential. However, Pazdur agreed to discuss the agency's new standards.

"A level playing field for all sponsors independent of *where* they perform trials or with *whom* they perform trials should exist," Pazdur said in an email. "Most importantly, the American public must have confidence that the same level of review, certainty and quality exists in all our product labels irrespective of sponsor, location, or clinical trial group."

The change is needed because the agency is increasingly willing to accept drugs based on delay in progression, as opposed to survival, Pazdur said.

"The FDA has generally viewed a survival improvement as an unambiguous endpoint that is not subject to bias," Pazdur said. "With radiographic endpoints, such as time-to-progression or progression-free survival, bias can be introduced, especially in unblinded trials. Our increasing use of radiographic endpoints rather than survival mandates a different level of scrutiny of an application and its endpoint."

Public vs. Industry Trials

The new requirements would mean that the cost of clinical trials submitted to FDA by the groups has just gone up by millions of dollars at a time of shrinking appropriations for NCI and cuts in the institute's clinical research funding.

This will affect a subset of trials: those that measure time to progression and could potentially be used to seek approval.

"We are already getting comments on protocols that are in development from the [NCI Cancer Therapy Evaluation Program], saying that this protocol has PFS as an endpoint, please provide a plan for conducting independent radiologic review of that endpoint," said Richard Schilsky, chairman of Cancer and Leukemia Group B. "So now we have to come up with a plan."

Chairmen of cooperative groups have varied opinions of the change.

"Up to this point, the cooperative groups have worked very closely with NCI and with industry partners in looking at questions that might not necessarily be the most important question to industry," said ECOG Chairman Robert Comis. "We come up with results that explore new indications, explore new ways to do things, and that needs to be protected for this country.

"It would be very difficult in the current federal budgetary NIH and NCI funding climate for the cooperative groups to basically do studies as if they were an industry trial," Comis said. "I am not sure where the resources would come from to do studies in that way. On the other hand, the way we do studies is high quality, rigorous, reproducible, and used by the world. I would hope that a high-level discussion among the cooperative group chairs, the NCI, the FDA and companies can be engaged to make sure that this system still provides the opportunity for the American public and cancer patients to benefit from the work of both the private system and the public system."

CALGB's Schilsky said he accepts the rationale for central review.

"From the groups' point of view, it's hard to argue with the FDA's position with respect to the scientific quality of data that have this kind of endpoints," said Schilsky. "We just need to know what the rules are, and then we will figure out a way to comply."

Jan Buckner, chairman of North Central Cancer

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Treatment Group, agreed. "The cooperative groups have a high quality standard, and we should never argue with getting the highest reasonable standard," he said. "The only issue is expense."

Buckner said the groups' external audits currently review only a fraction of images taken at member institutions. "There is external review of 10 percent of images from any particular institution," Buckner said. "It's not 100 percent. We could argue about whether you need to audit 100 percent in order to assure quality."

Some of the funds for central review could come from the industry, Schilsky said.

"The companies could fund it on a study-by-study basis," he said. "Various companies could contribute to some fund that is used to establish a central radiologic review program for the entire cooperative group system."

Pazdur said the changes in oncology have made it essential to apply the same set of standards to all players. "The need for uniform standards in clinical trial data quality gains increasing importance as greater numbers of commercial sponsors seek indications held by competitors," he said. "One sponsor's supplemental NDA may be another sponsor's first indication to receive marketing authorization. The rigor of the FDA clinical review should be similar both for the product's initial indication and any supplemental NDA. The public confidence in the reported results in the product label should be the same."

Another emerging trend is the increasing internationalization of clinical trial enrollment, Pazdur said.

"Most commercial sponsors are international organizations and conduct large international trials for registration," he said. "Large trials—such as adjuvant trials—that were considered the exclusive domain of the cooperative groups can now be performed by the pharmaceutical industry by conducting international trials.

"The quality of this data from international sites has been excellent."

Ultimately, the sponsor—not the cooperative group—is responsible for preparing the filings with FDA, Pazdur said.

"We strongly encourage a meeting with the FDA, commercial sponsors and *all* parties that will be involved in the trial's design, execution, and interpretation," he said. "These end-of phase II meetings (or similar meetings) are industry standards and should be in place independent of who will conduct the trial. There should be prospective discussions and agreement of the trial design, data monitoring, data collection, and the need for external radiographic review of primary endpoints."

Not Designed for Registration

The ECOG trial wasn't designed for getting Avastin approved.

"This was designed as an NCI-sponsored, approved cooperative group study, and I think it's a great example of the synergy between the public and the private sides of the system," Comis said.

It was the sort of study few sponsors would want to pay for.

"Our investigators felt that in spite of the fact that there was a trial that appeared not to be positive in second or third line breast cancer, that it needed to be tested in front-line metastatic disease treatment," Comis said. "This is a study that the company might not have done for years. We did it in a very timely fashion."

Altogether, 685 patients enrolled in the trial, E2100, were randomized to receive paclitaxel with or without Avastin. Patients who were HER2-negative were enrolled, as were patients with HER2-positive tumors who had received prior Herceptin (trastuzumab) or were unable to receive Herceptin.

The trial was stopped early based on a clear improvement in progression-free survival. Patients who received Avastin-paclitaxel had progression-free survival of 10.97 months, compared to 6.11 months for paclitaxel alone. The hazard ratio was 0.498 (CI: 0.401-0.618), and the p value was less than 0.001.

"The result of the study was apparent at the first interim analysis, because of the power of the effect, and so we made it known to the oncology community," Comis said.

The company submitted a supplemental Biologics License Application last May.

On Sept. 11, FDA sent the company a "Complete Response Letter," requesting confirmation of progression.

"The FDA has communicated to Genentech that they now expect the information from this cooperative group trial to be audited and summarized in a manner typically used for a company-sponsored trial," the company said in a statement. "This expectation is different from the understanding that Genentech had when the sBLA was submitted and will require the re-collection of information from ECOG study sites."

"We are disappointed that this will cause a delay in the review of our application, as there is a great unmet medical need for women with metastatic breast cancer," said Hal Barron, Genentech senior vice

president, development and chief medical officer, said in a statement. "Based on the scope of this request, we anticipate we will be able to resubmit the application to the FDA by mid-2007. We believe E2100 demonstrates significant clinical benefit and we will work with ECOG and the FDA to help bring Avastin to patients with metastatic breast cancer."

Miller and Comis said the information FDA requested can be provided.

"The chance of this happening by chance is astoundingly miniscule," Comis said. "I am absolutely certain that whatever is required will verify this result."

Miller said that, in principle, she shares FDA's concerns about investigator bias producing false results in assessments of disease progression. However, this concern has nothing to do with E2100, she said.

"If we had a two-month improvement or a six-week improvement, I would agree entirely, but that's not what we are talking about with this trial," Miller said. "No one has come up with a cogent explanation for how bias in a drug for which the bias of the time was this drug doesn't work in this disease gives you an over five-month improvement. That sort of requires a grand conspiracy of patients and physicians to continue a chemotherapy that they know is not effective for that patient and her disease for that length of time.

"I understand one assessment cycle, if everyone really believes this will work, but not for this amount of improvement."

Avastin is approved for the treatment of colorectal cancer and is listed in one of the reimbursement compendia as a treatment for first-line metastatic breast cancer. A delay in approval means that the company will be unable to market the drug for breast cancer.

Industry:

Bristol-Myers Board Ousts CEO Dolan Over Plavix Deal

By Paul Goldberg

The board of directors of Bristol-Myers Squibb Sept. 12 ousted the company's CEO Peter Dolan, ending a five-year tenure marked by a series of business missteps and scrapes with the law.

On Dolan's watch, Bristol, once the business and political pillar of oncology, has lost more than half of its shareholders' equity and has been reduced to operating under close surveillance by federal and state law enforcement officials.

It was, in fact, this monitoring of the company's efforts to delay introduction of a generic version of the blood-thinner Plavix that resulted in Dolan's downfall.

Bristol is still pledging to protect Plavix, the company's top-selling drug, which had net sales of $3.8 billion last year. Bristol sells Plavix in the U.S., and Sanofi-Aventis, the holder of the principal patent for the drug, has worldwide rights. The drug's global sales were $5.9 billion.

In March, Bristol and Sanofi made a deal with the Canadian generic drug maker Apotex Inc. that was preparing to launch a generic version of Plavix.

However, Bristol's deals were subjected to unusual scrutiny. To settle a civil action stemming from its efforts to extend market exclusivity for the cancer drug Taxol and the anti-anxiety drug BuSpar, in 2003 Bristol submitted to monitoring by state attorneys general and FTC.

In May, the regulators nixed the deal under which BMS and Sanofi were to pay Apotex $40 million to delay the market introduction of the generic Plavix until 2011, after the drug goes off-patent. Regulators also objected to Bristol's promise to refrain from launching an authorized generic version of the drug for six months, giving Apotex six-month exclusivity over the generic market.

The companies returned to negotiations, and a new agreement was framed last May, at a face-to-face meeting between the long-time Bristol operative Andrew Bodnar, and Bernard Sherman, chairman of Apotex. According to an Apotex court filing, Bodnar, an attorney and physician who serves as Bristol's senior vice president for strategy and medical and external affairs, made several oral side deals with the generic.

The filing states that Bristol and Sanofi insisted that "the side agreements not be included in the written agreement" in order to evade review by the FTC and the attorneys general. The Apotex filing is posted at www.cancerletter.com.

In the written portion of the agreement, Bristol made two concessions that were to come into play in case FTC and the attorneys general rejected the deal:

—Bristol agreed not to seek a temporary restraining order for five business days, in effect allowing Apotex to ship generic Plavix.

—Also, Bristol agreed not to seek treble damages in case the deal with Apotex failed and the company proceeded to sell a cheaper version of Plavix.

Federal officials took the Apotex claims seriously enough dispatch FBI agents to search the BMS executive

offices—including Dolan's—on July 27, and have launched a grand jury investigation of the deal.

Apotex Flooded Market With Generic

The criminal investigation was only a part of the debacle.

Taking advantage of Bristol's agreement to refrain from seeking a restraining order for five days, Apotex flooded the U.S. market with the cheaper, generic version of Plavix, which is now stockpiled by wholesalers.

On Aug. 31, a federal judge granted an injunction that precluded Apotex from selling the generic, but ruled that the drugs that had already been delivered could be sold legally. The judge noted that BMS and Sanofi had "agreed not to seek an injunction for a limited period of time during which Apotex concededly was permitted to sell its generic," and it was not up to the court to strike down that deal.

The ruling by Judge Sidney Stein of the US District Court for the Southern District of New York is posted at http://www.nysd.uscourts.gov/courtweb/pdf/D02NYSC/06-03453.pdf.

The five-day grace period allowed Apotex to ship enough Plavix to undercut Bristol's sales for about a year, causing Bristol to lower its projected earnings by up to 25 percent.

Industry observers said the two clauses in the agreement—the five-day grace period and foregoing of treble damages—were material events that likely should have been reported to investors. They were not.

After the FBI raid, the Bristol board acknowledged that Justice had launched a grand jury investigation of the Plavix deal, but denied wrongdoing by the company staff. "The Board has… directed that all BMS employees cooperate with the grand jury on this important matter," said the statement dated Aug. 17.

However, in that statement, the BMS board said that its internal investigation by an outside counsel indicated that no "unlawful conduct by BMS employees has been committed." The board said that after the matter surfaced in late July, it retained an attorney to investigate the allegation and another attorney to advise the board on "corporate governance and related matters."

On Monday, Sept. 11, the board met to hear a report stemming from that investigation. In addition to board members, the meeting was attended by retired federal judge Frederick Lacey, a court appointed monitor, and the U. S. Attorney for New Jersey Christopher Christie. To settle a channel-stuffing case last year, the company accepted a "deferred prosecution agreement"—essentially probation—with Christie's office, and therefore is monitored by Lacey. Dolan didn't attend the Sept. 11 meeting.

Addressing the board, Lacey made a "preliminary recommendation" that Dolan and general counsel Richard Willard be fired. Willard, former chief of the Justice civil division, was named general counsel last October.

According to the company statement, "Lacey's recommendation followed an inquiry by the monitor and the U.S. Attorney into issues related to corporate governance in connection with the negotiation of a settlement agreement of the pending Plavix patent litigation with [Apotex].

"The monitor and the U. S. Attorney did not find that there had been any violation of the deferred prosecution agreement. No finding of any unlawful conduct by the company or any of its employees has been made. The inquiry did not involve any matters that are the subject of the ongoing investigation by the Antitrust Division of the Department of Justice into the Plavix settlement agreement. The monitor may make additional recommendations with respect to governance matters when he makes his final report on the inquiry.

"The company's outside counsel conducting an ongoing internal investigation relating to the Plavix matter also confirmed that there is no evidence from which to conclude that the company or any of its employees acted unlawfully."

The BMS board statements are posted at www.bms.com.

A Bristol spokesman said Bodnar remains in his job with the company.

Cornelius Named Interim CEO

BMS board member James Cornelius, former board chairman and interim chief executive officer at Guidant Corp., was appointed to replace Dolan on an interim basis. Willard will be replaced temporarily by Sandra Leung, Bristol vice president and corporate secretary. Leung will be advised by former FBI Director Louis Freeh, a board member, the statement said.

Dolan, whose departure became effective immediately, is a member of the board of directors of C-Change and chairman of the board of the Pharmaceutical Research and Manufacturers of America. On Sept. 12, his photo portrait was taken down in the PhRMA lobby in Washington.

According to a C-Change spokesman, Dolan remains on the board of that organization.

Investors reacted by bidding up the price of Bristol shares by 93 cents, to $24.32 on Sept. 12.

Washington Roundup:

Two Republicans Vow To Block FDA Commissioner Nomination

Two Republican senators said they will block the nomination of Andrew von Eschenbach as FDA commissioner, The New York Times reported Sept. 15.

Sen. David Vitter (R-La.) told the Times that he will block the nomination if the Bush administration doesn't develop a "meaningful" program to legalize imports of prescription drugs from Canada or other countries.

Sen. Jim DeMint (R-S.C.) said he will block the nomination unless FDA takes steps to remove the abortion drug RU-486 from the market.

FDA is unlikely to take any action soon to meet these conditions. Von Eschenbach's nomination was blocked for several months by Sen. Hillary Rodham Clinton (D-N.Y.), and Sen. Patty Murray (D-Wash.) who demanded that FDA act on an application to allow over-the-counter sales of the emergency contraceptive Plan B.

FDA approved Plan B last month. Sen. Michael Enzi (R-Wyo.), chairman of the Senate Health, Education, Labor and Pensions Committee, scheduled a committee vote on the nomination for Sept. 20. After the committee vote, senators can issue holds that block the Senate from considering the nomination.

Any hold could cut von Eschenbach's chances of confirmation until next year, when Bush could renominate him, or make a recess appointment.

* * *

Mark McClellan last week confirmed his plans to resign as administrator of the Centers for Medicare & Medicaid Services next month.

McClellan ushered in the Part D prescription drug plan. President Bush said McClellan "bettered the lives of millions of Americans."

No successor has been named.

In the Cancer Centers:

Craig Thompson To Direct Abramson Cancer Center

CRAIG THOMPSON was named director of the Abramson Cancer Center of the University of Pennsylvania and associate vice president for cancer services of the University of Pennsylvania Health System**.** Thompson will direct all clinical divisions of the ACC, overseeing 300 cancer researchers and 299 full-time physicians and faculty from eight schools and 41 departments involved in cancer prevention, diagnosis, and treatment. He will be responsible for $180 million in grant funding for cancer research and training, including $83.4 million in NCI funding. His additional clinical duties will include heading the PENN Medicine Cancer Steering Committee and the University of Pennsylvania Cancer Network, said **Arthur Rubenstein**, executive vice president of the health system and dean of the School of Medicine, University of Pennsylvania. Thompson joined Penn in 1999 as professor of medicine, scientific director of The Leonard and Madlyn Abramson Family Cancer Research Institute, and is the first chairman of the Department of Cancer Biology. He will continue to serve in both positions. . . . **V. CRAIG JORDAN** has received a $10.7 million grant from the Department of Defense Breast Cancer Research Program for a breast cancer center of excellence. He is vice president and scientific director of medical science at Fox Chase and the Alfred G. Knudson Jr. Chair in Cancer Research. The center of excellence would develop a treatment model that reverses the eventual development of resistance to anti-estrogen therapy. The five-year multidisciplinary project, which encompasses both laboratory research and clinical trials, involves scientists and physicians at Fox Chase and Lombardi Comprehensive Cancer Center, Georgetown University, Translational Genomics Research Institute in Phoenix, and Johns Hopkins University. **Lori Goldstein**, director of the multidisciplinary Breast Evaluation Center at Fox Chase, is co-principal investigator for the grant. "The centerpiece of our effort is the clinical trials consortium enhanced with consumer advocate participants from the Y-Me National Breast Cancer Organization, the Susan G. Komen Foundation, National Breast Cancer Coalition and Research Advocacy Network," Jordan said. "We will rapidly export our preliminary clinical finding to the Eastern Cooperative Oncology Group, which will establish the dose of short-term estrogen treatment necessary to be given to patients.". . . **MARK MORGAN** was named chief of gynecologic oncology at Fox Chase Cancer Center. Morgan's clinical interests include complex gynecologic surgery and the surgical management of gynecologic malignancies. He came to Fox Chase's surgical oncology department from the University of Pennsylvania Health System, where he was a professor in the division of gynecologic oncology. He was also the founder and director of the division of urogynecology and female reconstructive pelvic surgery. He also was principal investigator of the Gynecologic Oncology Group while at Penn.

NCI Programs:

Centers Urge Application Of Prevention, Early Detection

(Continued from page 1)

Eschenbach's emphatic belief in the literal achievement of the 2015 goal.

"Last November, we were meeting with Dr. von Eschenbach, and there were some heated discussions about the 2015 target," Mendelsohn said in presenting the report to the NCAB. "What was brought out in that discussion was that a great deal has been accomplished, and a great deal can be done, and let's focus on that rather than trying to put a due date in saying everything that must be accomplished. Let's develop a time line and get working on it."

NCI's decreasing budget also prompted action, Mendelsohn said. "We were very frustrated with the reduction in NCI funding at a time when there is such opportunity," he said. "I should give Dr. von Eschenbach credit for this. I think his last gift to us was to stimulate us to realize that by working together in a collaborative way, we could exert tremendous leadership and pressure to accomplish the goals that we all share. We are a very powerful force. We represent a majority of the states in the United States, and we represent a substantial part of the spending as a result of NCI grants."

The center directors concluded that, "We can reduce deaths from cancer and we can substantially reduce them more by applying what we know today, mostly in the area of early detection and prevention," Mendelsohn said. To increase public awareness, NCI could use its "very strong publicity group" to "remind the American people that if you are 85 or under, this is the most common cause of death in our country," he said.

The report cites the American Cancer Society's recent analysis of progress toward its goal of reducing cancer deaths by 50 percent between 1990 and 2015. "If trends over the past 12 years continue, the projection is for a 23 percent reduction in cancer deaths by 2015," the report said. "However, for breast cancer, colon cancer, and lung cancer in males, the trends predict a 50 percent reduction."

The 70-page report includes recommendations for prevention, early detection, treatment, survivorship, collaborations, and dissemination. The directors endorsed the recommendations of the National Cancer Policy Board on cancer prevention and early detection, as well as the Clinical Trials Working Group report on improving NCI's capacity to lead clinical research.

The report, "Accelerating Successes Against Cancer, Recommendations from the NCI-designated Cancer Center Directors," is available at http://www3.cancer.gov/cancercenters/Accelerating_Successes_Against_Cancer_Report.pdf.

Decreasing The Burden of Cancer

NCI Director John Niederhuber said the institute would work to implement the report's recommendations.

"Our responsibility is to see how much of this we can accomplish," he said to the NCAB. "If we continue to work on this as a group over the coming years, I think we can accomplish a lot that will make it possible to get to the outcome we want, that is, decreasing the burden of this disease."

NCI should work through the Association of American Cancer Institutes to implement the recommendations, Niederhuber said. "Sometimes it's lost that we invest in 61 centers, but there are another 20 centers that we don't invest in that also perform very much like the 60 centers that we invest in," he said.

NCAB Chairman Carolyn Runowicz, director of the Neag Comprehensive Cancer Center at University of Connecticut Health Center, called the report's recommendation that the centers share their resources "historic."

Support for the cancer centers sometimes wanes at NCI, said NCAB member Donald Coffey, professor of urology at Johns Hopkins University School of Medicine. "The biggest bang by far that the NCI and the nation gets in cancer is the investment in cancer centers, which totally revolutionized things, and second, the Organ Systems Program, which got killed by the NCI, which gave us PSA, and third, the SPOREs, which brought everybody together. Now those are under fire. I sometimes feel that those are under fire from the NCI. They're not now…. I think the cancer centers are the heart of the NCI."

NCI should fund more research in the molecular and cell biology of the cancers that remain difficult to treat and have low survival rates, Coffey said. Also, while the field of nanotechnology currently is "red hot," the technology could be limited for use in humans by the spleen, which filters the compounds, he said. "I think we have to get a heads-up in studying those things before they actually hit us," he said.

NCAB member Kathryn Giusti, CEO and founder of the Multiple Myeloma Research Foundation, said the NCI funding decrease has escaped notice outside of cancer research. "The public doesn't think we have

a crisis," she said. "Many times we go out and speak with major philanthropists and they don't realize we have a crisis in cancer."

Giusti also cautioned against overstating "personalized medicine," a phrase used increasingly at cancer meetings. "While you can talk about personalized medicine in breast cancer, we are getting killed when I meet with philanthropists who say, 'I'll give you a million dollars if you can find some cell lines and cure my disease.' I have to say no. We turn that money down, but I will promise you that the person did go to an academic center who promised they will help them. We have to be careful about what we're promising in personalized medicine, because we are not there yet, or even close, in many diseases."

Collaboration among cancer centers "is driven by money," said Giusti, whose foundation supports a consortium of 11 centers. "When push comes to shove, our collaboration is driven by the fact that people know we have money and access to tissue and access to data," she said. "I think it is critically important that we see collaboration across the cancer centers, especially in the uncommon cancers. Collaboration is driven by money and tissue, but it's also driven by process."

NCAB member Bruce Chabner, clinical director of the Massachusetts General Hospital Cancer Center, said progress against cancer is slowed by the months it takes for clinical trials to be reviewed and approved.

"We have a serious problem nationally in the time that it takes to get a protocol reviewed and activated in our cancer centers," Chabner said. "It takes five months in our center. It's not a problem of money, it's a problem of national policies, or absence of national policies about how protocols should be reviewed and activated.

"We find that when we're site visited, we're told to add a lot of additional layers of review and scrutiny of our protocols, which is often totally useless, because these have gone through cooperative groups and multiple levels of discussion," Chabner said. "If we thought about this like a drug company, time is precious in terms of getting these drugs into process and getting them to patients."

Federal agencies that put the regulations in place should review procedures, said Martin Abeloff, director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, who served on the center directors committee. "It takes six months to a year to get one regulatory thing done," he said. "The latest is the Medicare reimbursement for patient care costs in clinical trials. A simple statement at one or two meetings by a Medicare official had our regulatory office change everything that we were doing, because there already have been multi-million-dollar settlements on this."

CHABNER: "It's not an issue of money. If NCI could coordinate a common policy among the cancer centers and industry about how we should be reviewing and activating our trials, and cut that time down to something reasonable, the benefits to the cancer community would be remarkable."

MENDELSOHN: "Bruce, I agree with you and I have thought about this a lot. One of the main problems is that the federal government's position on all of these issues is, never make a mistake. If you're going to pass laws for privacy that make it almost draconian to try to use tissue specimens and study them, because we don't want to invade privacy. It's hard to take someone who is dying of lung cancer that is going to be dead in two months, unless God intervenes with a miracle, and say let's be sure we don't give them a new drug that might hurt them."

CHABNER: "So who are they protecting? Cancer patients themselves want this process to be faster."

James Doroshow, director of the NCI Division of Cancer Treatment and Diagnosis, said the institute could look "quite urgently" at Cancer Center Support Grant guidelines to reduce duplicative protocol review.

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