THE CANCER LETTER

Vol. 30 No. 19
May 7, 2004

Specter of Iressa Lingered Over ODAC As It Voted Down Genasense And RSR13

By Paul Goldberg

Soon after the lung cancer drug Iressa was approved by FDA, an intriguing hypothesis emerged on Wall Street and in the pharmaceutical industry.

The agency has become willing to accept therapies that have low efficacy, yet seem to help a few individuals dramatically, observers said. In the case of Iressa, which received accelerated approval, the response rate was 10 percent in a single-arm study.

The shadow of Iressa (gefitinib) lingered over the May 3 meeting

(Continued to page 2)

In Brief:

Panel Nixes Stock Options For NIH Employees; Le Beau Directs U. of Chicago Cancer Center

NIH employees who engage in work outside the institutes should not receive compensation in the form of stock options or equities, an advisory panel recommended in its report this week. The panel said such compensation would make NIH employees, in effect, owners of the company, potentially resulting in "a conflict of commitment as well as interest," the report by the Conflict of Interest panel said. Co-chaired by National Academy of Sciences President **Bruce Alberts** and National Academy of Engineering member **Norman Augustine**, the panel reviewed existing laws, regulations, and policies that govern public disclosure of financial conflicts-of-interest by NIH staff. The panel's report is available at www.nih.gov/about/ethics_COI_panelreport.htm. . . . **MICHELLE LE BEAU** was appointed director of the University of Chicago Cancer Research Center. Le Beau is professor of medicine in the Department of Medicine Section of Hematology/Oncology, the Committee on Genetics, and the Committee on Cancer Biology, of which she has been chairman since 2000. She has been program leader for the Molecular Genetics and Hematopoiesis Program in the Cancer Center as well as director of the Cancer Cytogenetics Laboratory. Le Beau served as the head of cytogenetic studies of lymphoma for the Children's Cancer Group for nearly 10 years, and was a member of the Cytogenetics Review Committee for Cancer and Leukemia Group B. . . . **ONCOLOGY NURSING SOCIETY** elected new officers. **Karen Stanley**, a nursing consultant in cancer care issues with special interests in pain and symptom management, end-of-life care, and geriatric oncology, became president, succeeding **Judy Lundgren** for a two-year term. **Laura Benson,** director of medical communications

(Continued to page 8)

ODAC Turns Down Two Drugs For Melanoma, Brain Mets

(Continued from page 1)

of the FDA Oncologic Drugs Advisory Committee, as the advisory board considered the applications for two drugs that fell short of presenting a slam-dunk case: Genasense (oblimersen sodium), a front-line metastatic melanoma treatment sponsored by Genta Inc., and RSR13 (efaproxiral sodium), a brain metastasis treatment sponsored by Allos Therapeutics Inc.

To FDA-watchers, these were more than ordinary drugs. They were a test case of sorts, the first two therapies that went to ODAC since Sept. 24, 2002, the day committee recommended approval of Iressa. Watching ODAC turn down both drugs this week left observers wondering whether the Iressa precedent has been overinterpreted and whether it was a precedent at all.

"I don't think that there is any question that Iressa changed the way the companies perceived the whole regulatory process," said Michael Hart, president and CEO of Allos Therapeutics. "To this day, you talk to clinical oncologists, and they will tell you, `Hey, if you can get a 10 percent response rate in patients that have failed everything in non-small cell lung cancer, that's good enough.'"

The industry came to believe that the FDA process had changed, Hart said. "The message that came out is that dealing with FDA is one thing, but if you can get before ODAC, then you have the possibility of talking clinician-to-clinician and really trying to point out the clinical effect the drug is having on patients with whatever disease they have," Hart said.

The message of the May 3 meeting was different. "What we saw in our meeting is that FDA didn't allow it to get that far, because they stayed on the statistical issue," Hart said.

Interviews with committee members suggest that the significance of the Iressa phenomenon may have been greatly exaggerated.

"People thought the bar has been lowered," said ODAC member Silvana Martino, a breast cancer expert at the John Wayne Cancer Institute-St. John's Health Center in Santa Monica, Calif. "I think the way things have been translated is that the response rate for Iressa was quite low. The committee voted to approve that drug, and I suspect that people took that and translated that into that our goals and ethics had changed, and just about anything could get through ODAC."

The nixing of Genasense and RSR13 was consistent with the vote on Iressa, said ODAC member John Carpenter, professor of medicine at the University of Alabama at Birmingham. "I don't think we eased the standards," said Carpenter, whose term on the committee ended at the most recent meeting. "We were asked the very same questions. I think what was clear on Iressa was that there was something real going on. We just didn't know how much. With these drugs, we didn't have any idea whether there was anything real going on."

While many observers attributed the Iressa approval to the efforts by former FDA Commissioner Mark McClellan to make the agency more receptive to the industry, it is unlikely that the majority of ODAC members would recognize McClellan if he walked into a room without a nametag. Committee members said FDA employees had no influence on their decision on Iressa, Genasense, RSR13, or any other agent.

"Nobody from FDA ever said anything to me one way or the other," said Otis Brawley, associate director for cancer control and professor of medicine at Emory University's Winship Cancer Institute. "The only people who ever approached me and tried to lobby for my vote on Iressa were advocates exercising their free speech rights. I felt absolutely no pressure on that vote."

Brawley said he changed his mind five times before casting a vote for Iressa, and his vote would have been "No" had the drug been associated with greater toxicity or if it required more cumbersome administration, he said.

Martino said the pressure she felt was generated only by the data before her. "People will always choose

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

www.cancerletter.com

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
E-mail: news@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
E-mail: info@cancerletter.com

Subscription $315 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

to believe what suits their personalities and their needs in life," said Martino, whose term on the committee has ended. "I can tell that from my own experience with ODAC, it is an extremely independent group of people. None of us even discuss these issues with each other. So what you see on the day when you see us sitting there is, in fact, the reality of the experience. I can tell you from the depth of my heart, there is no bias. And most of us aren't really swayable by either side. To me, it's not the issue of sides. To me, it's the issue of responsibility. What is the responsibility of the medical field of which the FDA, and ODAC, and the pharmaceutical companies and the physicians are part of? What is our goal here? And I can't imagine that our goal can be that we approve therapies where I am scratching my head, trying to figure out if they are doing anything at all."

The decision to approve Iressa was controversial (**The Cancer Letter**, May 9, 2003). However, recent discovery of mutations that correspond to response to Iressa is likely to help define populations of patients who would be likely to benefit from the drug, thereby greatly enhancing the response rate and, presumably, benefits to patients (**The Cancer Letter**, April 30).

Iressa And The Value of Testimonials

While testimonials by patients helped Iressa, they didn't help Genasense.

FDA has been under pressure from some advocacy groups, the pharmaceutical industry, and the writers from The Wall Street Journal editorial page to relax its requirements for approval, particularly in oncology.

The Genasense presentation began with an appearance by Rep. Peter Deutsch (D-Fla.) and the reading of a letter from Rep. Mike Ferguson (R-NJ). Both serve on the House Committee on Energy and Commerce and its Subcommittee on Oversight and Investigations.

"I am not a physician or a scientist," Deutsch said to ODAC. "And I have not studied the clinical data regarding this drug. But I do know this: If you find that this drug is as safe and effective as other available treatments—if it reasonably presents another possible course of treatment—by what right can government deny cancers patients an avenue to save their lives? This is not about a passing illness for which there are other treatments. This is about cancer; an absolutely devastating disease that has, in some way, affected nearly every single American. This is about cancer patients who are dying and are desperate for the chance to live longer. It is their interests that must be foremost today."

After reading the statement, Deutsch left to catch a plane back to Florida, where he announced a campaign for a Senate seat. However, a phalanx of Energy and Commerce staff members remained in the front row throughout the Genasense presentation. With Congressmen included, 15 supporters came to an open mike to offer testimonials, matching the Iressa record (**The Cancer Letter**, Sept. 27, 2002).

ODAC members said they weren't intimidated by political muscle. "I suspect that they either have personal concerns, or they are responding to their constituents' concern," said Carpenter. "[Deutsch] gave all this song and dance, and said, 'I hope you will look carefully at this drug. If you think it's worthwhile, approve it.' It's hard to object to that. As long as he doesn't push the committee to do something based on some reason other than the real results, I don't think it's a big deal. As long as they speak publicly and they ask you to do the right thing, I don't think it's a serious problem."

Another committee member said he cringed at Deutsch's discussion of his basal cell carcinoma—a disease that is trivial compared to melanoma. However, the appearance had no impact on his decision, the committee member said.

"I would accept that ODAC was floored by the number of people who had third-line chemotherapy for lung cancer who showed up and said, 'Iressa has helped me,'" said Brawley, who didn't take part in the Genasense and RSR13 discussion, but agrees with the outcome. "That was much more impressive than the Congressmen."

Trials Didn't Meet Primary Endpoints

Setting the tone for the May 3 meeting, Richard Pazdur, director of the Division of Oncology Drug Products in the Center for Drug Evaluation and Research at FDA, focused on the similarities between the Genasense and the RSR13 applications.

Had Pazdur chosen to extend his remarks to Iressa, he would have touched on another crucial difference between the AstraZeneca drug and the two therapies that were placed before ODAC that day. Iressa received an accelerated approval as a single agent in the third-line indication. This allowed ODAC to disregard two negative studies of Iressa as part of a combination therapy in the front-line.

Since Genasense and RSR13 didn't meet the primary endpoints in the study population for which they sought approval, they weren't eligible for accelerated approval. Thus, while Iressa received an accelerated approval based on tumor shrinkage as a surrogate for

patient benefit, the sponsors of Genasense and RSR13 had to demonstrate a tangible benefit to patients.

The text of Pazdur's opening remarks follows:

"This morning's meeting focuses on a drug for the treatment of patients with advanced melanoma who have not received prior chemotherapy. I would like to spend some time addressing issues for you to consider during the presentations provided by the sponsor and the FDA staff.

"These issues are important to this application, but also this afternoon's application, and drug development in general—especially, as we have continuing ongoing discussions and dialogue with the committee on endpoints for drug development.

"The FDA has long considered the demonstration of improved survival as the gold standard for drug approval. An improvement in survival associated with an acceptable safety profile is of unquestionable clinical benefit. It is assessed daily and is unambiguous.

"When we at the FDA began our discussions with the committee on endpoints for drug approval, we realized that there may be some disadvantages to requiring a survival improvement for drug approval. These disadvantages include the confounding of survival analysis by crossover of therapy, large patient numbers required to be enrolled on trials for survival, and the long follow-up that may be required in selected oncological diseases.

"This trial at hand this morning [Genasense] was originally discussed with the agency to be a trial with a primary endpoint of survival improvement. The trial did not demonstrate an improvement in overall survival. We are asked to evaluate this drug for approval on the bases of secondary endpoints of claimed improvements in progression-free survival or progression-free survival and response rates.

"Please remember that since the drug is added to a standard therapy, we must assess the drug's contribution to that standard therapy, and any claimed response rates or claimed PFS advantages represent a combination of the investigational agent and the standard therapy. Hence, we must isolate the effect of the drug in assessing the drug's efficacy.

"Let's turn our attention to the measurement and assessment of progression-free survival. The assessment of PFS may be difficult and uncertain in an unblinded trial with a small effect on this endpoint and where there is a lack of attention to clinical trial issues that are important in measuring and comparing PFS data between treatment arms.

"These issues include a prospectively defined methodology for assessing, measuring, and analyzing PFS. These need to be detailed in the protocol and the statistical plan. Tumor progression should be carefully defined in the protocol. The FDA and sponsor should agree prospectively on the protocol, case report forms, and statistical plan. Tumor progression should be carefully defined in the protocol. FDA and the sponsor should agree prospectively on the protocol, the case report forms, and the statistical analysis plan for PFS.

"There should be a pre-specified analysis planned for handling missing data—especially missed assessment visits. Censoring methods and assessment of progression in non-measurable lesions must be prospectively outlined and agreed upon. Most importantly, visits and radiological assessments should be symmetrical on the study arms to prevent systematic bias.

"When possible, studies should be blinded—especially important when the patient or investigator assessments are included as components of the progression endpoint. If progression is assessed by both the treating physician and an external radiology committee, the protocol should prospectively stipulate whose assessment will be used in defining PFS. This cannot occur after the study data had been examined.

"Hence, from a practical perspective, PFS, as a primary endpoint for drug approval, takes meticulous, prospective planning. The measurement of PFS requires rigor. This planning is frequently lacking in clinical trials that relegate PFS to a secondary endpoint. Some practical problems outlined above in accurately characterizing the treatment effect on PFS will be discussed by the FDA reviewers.

"Provided an acceptable safety profile, one has to answer the following question: What is the magnitude of the drug's effect on PFS that would be considered clinically relevant? A very small effect may raise questions about the very existence of the effect, especially when the study is unblinded and attention to the symmetry of assessments and handling of missing assessments is not evident.

"In answering whether marketing approval should be granted to an agent, two important questions need to be answered. First, does the drug have a convincing effect that can be adequately characterized? Secondly—and this question can only be addressed if the first question is answered in the affirmative—what is the clinical relevance of the effect?

"This obviously must take into account a risk-benefit analysis. Benefit can only be assessed in this equation if it convincingly exists and can be adequately characterized.

"I hope these comments will provide a catalyst for your consideration this morning, this afternoon, and tomorrow."

Genta submitted an unblinded phase III study of 771 patients randomized to receive Genasense plus dacarbazine (DTIC) or DTIC alone as first line therapy for metastatic melanoma. The primary endpoint was survival. The study showed no survival improvement for the Genasense and DTIC arm, and the advantage in PFS was less than a month, FDA said. Also, the agency was concerned about response assessment and bias that can occur in an unblinded study.

Allos submitted a phase III trial comparing whole brain irradiation with RSR13 as an adjunct to whole brain irradiation as a treatment of brain metastasis in 538 patients. Patients with non-small cell lung cancer and breast cancer brain metastases were enrolled. The trial didn't meet the overall survival endpoint, and the company sought approval based on a non-prespecified subset of 115 breast cancer patients. A large randomized trial based on this subset analysis is in progress.

"The Other Drug"

The specter of "the other drug" emerged soon after the committee began discussion of Genasense.

"My concern is that if we consider this unapprovable, this drug is going to die, and we will never figure out how to use it and how to apply it better, and how to study it better in other diseases, as well as melanoma," said ODAC member Bruce Cheson, head of hematology at Georgetown University Lombardi Comprehensive Cancer Center. "When I sat here at another ODAC meeting, I saw another drug approved with a response rate in which the lower limit of the confidence interval was 5.4 percent, and there were two huge negative phase III trials. To me, these results are a lot more encouraging than the drug that was approved.

"I have no conversations with the company, but when a small company that has devoted a lot of resources into a particular drug, and it doesn't get approved, then, based on economics, etc., drugs tend to fail away."

Robert Temple, associate director for medical policy at the FDA Center for Drug Evaluation and Research and director of the Office of Drug Evaluation I, said concerns about the sponsors were extraneous to discussion.

"Not to state the obvious, but, really, we need to know from you whether the therapy works, not whether you feel bad for the company, feel bad for the state of oncology development," Temple said.

CHESON: "I think there is a strong signal here, but I think, as with that other drug, we don't know the optimal way to use it. But there is a signal here. I do believe that progression-free survival may be a better endpoint. And had this trial been started today instead of several years ago, they would have been recommended to use PFS."

TEMPLE: "This question is whether there is a difference in progression-free survival."

CHESON: "I'll vote yes on that when it comes my time to vote yes on that."

STEPHEN GEORGE [professor of biostatistics at Duke University Medical Center]: "To me, some of this is rather disturbing… There wasn't an advantage in survival. There may have been some signal there, that is a very small percentage of patients who achieve a CR may be long-term survivors and may in fact be really long-term. But to detect that kind of difference, of course, is very, very difficult. I think what's bothering me is that I am thinking, 'There might be something here,' but it just isn't clear. It's clear that overall survival wasn't significant. I am very suspicious of progression-free survival. I am very worried by the differential measurement timing, so when I look at response rates, I hear that this independent assessment of response rate. This might be a promising agent but at a very low level."

PAZDUR: "We first want to make sure that there is a biological effect. What is the effect of this drug on the endpoint, and how adequately characterized is that effect? We have to answer that question first, before we go to discussion of clinical relevance. The clinical relevance of a certain drug brings into the risk-benefit relationship. Benefit cannot be discussed unless it's adequately characterized."

SARAH TAYLOR, [an oncologist at the University of Kansas Medical Center, whose ODAC term has ended]: "I have concern about progression free survival, because there are some patients who have very slow growing tumors. If you are going to use that as a measurement, you have to know how rapidly they were progressing before they were treated. As a clinician, I have seen that melanoma is an unpredictable disease. Although its response to chemotherapy has been dismal, I have patients who were on tamoxifen studies and are now 20 years out."

GREGORY REAMAN, [professor of pediatrics at George Washington University and chairman of Children's Oncology Group]: "I regret that we've brought up the past, a prior meeting of this committee, but unfortunately it's been brought up. There was a reference to a response rate that was of a similar

magnitude. I feel that we are being called upon to make a similar decision again. Also, I am troubled by the fact that the response rates and the method for independent review were troublesome. I just feel that we are between a rock and a hard place."

PAZDUR: "Remember, the 'Other Drug,' that you mentioned here. That was a single agent that produced a 10 percent response rate. We are talking about a combination therapy, and we want you to take a look at that combination."

After reading the question that would determine whether the drug should be approved, ODAC Chairman Donna Przepiorka delineated Genasense from the other drug:

"I am a pro-PFS kind of person, with the exception of when the experiment is not done very critically," said Przepiorka, professor of medicine at the University of Tennessee, whose term on the committee has ended. "PFS has to be considered a valid endpoint in melanoma, for which there is no drug, which shows the benefit for survival. The other issue has to do with the administration. As it has been pointed out, Genasense is administered by continuous infusion requiring a pump and a catheter, and is not given as a pill."

The committee voted 13:3 against approval.

The FDA approval question read: "Do the results of this study, in particular the small difference in RR (<5%) and/or PFS for the combination of Genasense + DTIC versus DTIC alone, in the absence of a survival improvement, provide substantial evidence of effectiveness that outweighs the increased toxicity of administering Genasnse for the treatment of patients with metastaic melanoma who have not received prior chemotherapy?"

Later that day, the committee voted 16:1 vote against approval of RSR13 for brain metastasis. Here, the question read: "The survival analysis of the overall population was negative. Do the observed survival results from this single study in the subgroup of patients with breast cancer metastatic to the brain represent substantial evidence of RSR13 efficacy in this subgroup?"

The Effect of Pressure and Other Behaviors

Based on recent history, it appears that a date with ODAC doesn't indicate imminent triumph for a company.

More likely, it suggests that the agency has profound questions about the application, and that the company insists on throwing its fate to the jury. When a drug appears to be beneficial, the agency approves it without seeking advice from outside experts.

The onslaught of Wall Street Journal editorials and repeated attacks from patient groups appear to have forced the agency to explain its actions in layman's language. In an apparent effort to explain the likelihood of a thumbs-down vote on RSR13, the agency asked ODAC biostatistician George to present a brief lecture on "Subgroup Analyses in Clinical Trials."

This was a bad omen for Allos Therapeutics. "Maybe it was a misperception, but the industry wanted to believe that McClellan was having a distinct impact on how far FDA was willing to go to work with sponsors," said Allos executive Hart.

"We really didn't know specifically where ODAC was going," Hart said. "Companies spend a lot of money preparing their best case for ODAC. I think there is implied good faith going forward that while there may be disagreements over the data, you should have reasonable opportunities to defend your position in front of ODAC. Clearly, getting questions 10 minutes before you go in there doesn't allow you to do that.

"There were two questions. The second question we didn't get to, and the second question dealt with safety.

"We came to the conclusion that FDA had an agenda as it related to our application, and that is that they were going to use us as a poster child for all future companies even thinking about bringing a subgroup analysis before the FDA.

"Sponsors are always faced with how important is it to review drugs that deal with a patient population in which there hasn't been a standard of care for 40 years. In our situation, brain metastasis has been largely ignored. For that reason, we had two statistical paths outlined in the statistical analysis plan, both unadjusted log rank and Cox multiple regression.

"We had confounding results in unadjusted log rank and Cox as it related to the primary, the subgroup and breast patients. But the Cox was positive. The fact that it was positive, which FDA confirmed, led us to the breast cancer subgroup. There is no flaw in the logic as to how we got to the breast cancer subgroup. Unfortunately, the meeting didn't acknowledge that, and focused on the fact that, 'I can see how you got there, but we don't think that the sample size is large enough, or we don't think that the evidence is as compelling as it needs to be.' They, in fact, chose to just literally pile on these statistical arguments.

"There were maybe three or four comments from medical oncologists at all. It was a debate over pure statistics. From my perspective, as the CEO of this company, having to make sure that we adequately spend

our shareholders' money, the decision to go forward with filing the NDA in large part was based on a good-faith effort that you were going to get an opportunity to adequately defend your position. FDA doesn't need sponsors to spend $500,000 to prepare for a meeting, and convene an ODAC panel if they don't want any subgroup analysis to inform the basis of approval. All they have to do is just write this into the regulations. It could be one sentence in the regulations.

"To convene an ODAC panel to have Steven George give a tutorial on subgroup analysis, Statistics 101, is a total waste of taxpayers' money. It was obviously an attempt to drive home a point that might not have needed to be taken to that extreme in a public forum."

Hart said the Allos application was anything but a wild gamble. "This was not just Allos thinking, 'We are going to push the envelope here and go take on the FDA,'" he said. "Believe me, if we had any inkling at all of the outcome of that ODAC meeting, and the way it was run, and the way the questions were answered, we would have not filed an NDA."

The company's application was reasonable, Hart said."I can appreciate the agency's point of view on subset analysis, but this clearly was not data-dredging," he said. "This falls out of the Cox multiple regression analysis, which was a pre-specified statistical analysis tool. So, I think the take-home message for sponsors is that if you don't get your primary endpoint with your primary analytical tool, nothing else matters."

Had discussion proceeded beyond the question of subset analysis, the committee might have found a rationale for giving RSR13 an accelerated approval, Hart said. "The whole discussion over response rate in the brain could have very well led to that being considered as a surrogate endpoint likely to predict survival in the entire patient population," he said.

Endpoints For Approval

Continuing a systematic evaluation of criteria for approval of cancer drugs, on May 4, ODAC recommended standards for colorectal cancer.

The committee recommended unanimously (15:0) that in the adjuvant setting an increase in disease-free survival can represent a clinical benefit, when compared with standard therapy. An increase in DFS should be considered a benefit for a patient, and can serve as a basis for regular approval, ODAC said. DFS is defined as the time from randomization until either death or the recurrence of disease.

The committee also voted unanimously that progression-free survival should be a preferred surrogate endpoint, compared to time to progression, in the first-line setting for advanced disease. PFS measures the time to either disease progression or death, while TTP doesn't include death as an event in the analysis.

ODAC was less certain about the value of progression-free survival as a basis for regular approval in that setting. The committee voted 8:5 with one abstention to recommend the use of PFS as an endpoint for approval of a hypothetical drug regimen compared to a standard first-line regimen.

"The ODAC discussion underscores the need for careful planning and precise definitions in considering PFS as a basis for approval," said Steven Hirschfeld, oncology group leader at Center for Biologics Evaluation and Research. "The difference in PFS between study arms has to be substantial."

Pazdur said the agency is writing a series of guidance documents on endpoints for approval of oncology products. "The first guidance will be a general discussion of the advantages and disadvantages of specific endpoints," he said. "Subsequent guidances will focus on disease-specific issues."

In another action, ODAC reviewed a generation of new studies that have been started by Johnson & Johnson and Amgen Inc. as follow-up to recent findings of toxicity of erythropoietin (**The Cancer Letter**, Oct. 24, 2003).

The studies that brought the safety issue to the agency's attention sought to achieve hemoglobin levels that reach the normal range, and were greater than 12 gm/dL. Studies that will be performed by Amgen and J&J will seek to achieve hemoglobin in the range labeled for the U.S. market.

The agency is asking for a new generation of studies that would measure thrombotic and cardiovascular adverse events, tumor progression, and survival.

Funding Opportunities:

RFA Available

RFA-CA-05-017: Support for Human Specimen Banking in NCI-Supported Cancer Clinical Trials

Letter of Intent Receipt Date: June 21, 2004

Application Receipt Date: July 21, 2004

The initiative supports the infrastructure for the collection of, storage of, and access to high-quality, well-annotated human specimens collected from and representative of the patient populations entered into NCI-funded, phase III clinical treatment trials. Improving the quality and accessibility of specimens from NCI-supported clinical trials will facilitate the development of prognostic and predictive markers, molecular signatures, identification of therapeutic

targets and other important translational research studies. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-05-017.html.

Inquiries: Roger Aamodt, phone 301-496-7147; fax 301-402-7819; e-mail ra32u@nih.gov.

Program Announcements

PAR-04-096: Paul Calabresi Award for Clinical Oncology

Letter of Intent Due Date: June 1, 2004, May 2, 2005

Application Receipt Date: July 1, 2004, June 1, 2005

The purpose of the PCACO the career development of medical doctors in translational research who 1) perform clinical oncology therapeutic research that develops and tests scientific hypotheses based on fundamental and clinical research findings; 2) design and test hypothesis-based, clinical therapeutic protocols and adjunct biological analyses and for clinician candidates to administer all phases (i.e., pilot/Phase I, Phase II, and Phase III) of cancer therapeutic clinical trials, and (3) conduct cancer therapeutic research in team research settings in which basic and clinical scientists collaborate and interact to expedite the translation of basic research discoveries into patient-oriented therapeutic cancer research. The PA will use the NIH Mentored Clinical Scientist Development Program Award or K12 grant mechanism. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PAR-04-096.html.

Inquiries: Lester Gorelic, Cancer Training Branch, NCI, phone 301-496-8580; fax 301-402-4472; e-mail gorelicl@mail.nih.gov.

PA-04-102: Phased Application Awards in Cancer Prognosis and Prediction

NCI Cancer Diagnosis Program invites applications for a first phase R2 for technical development and a second phase R33 for application and evaluation of clinical utility. The first phase should demonstrate the technical feasibility of the study design proposed for the second phase, including the analytic performance of the assay or test system on samples comparable to those that will be used in the second phase. The second phase should test whether application of the strategy will provide clinical benefit to a defined set of cancer patients. The PA will use the Exploratory/Developmental Research Grant phase II R33 and the combined R21/R33 Phased-Innovation Award mechanisms. The PA is available at http://grants2.nih.gov/grants/guide/pa-files/PA-04-102.html.

Inquiries: Tracy Lugo, phone 301-496-1591, e-mail lugot@mail.nih.gov.--(for general inquiries and for projects related to breast cancer, lung cancer, gynecologic cancers, or brain tumors). Magdalena Thurin, phone 301-496-1591; e-mail thurinm@mail.nih.gov.--(for colon cancer, gastric cancer, pancreatic cancer, skin cancers including melanoma, sarcomas, or acute leukemias. James Tricoli, phone –301-496-1591; e-mail tricolij@mail.nih.gov.--(for prostate cancer, renal or bladder cancer, head and neck cancer, esophageal cancer, liver cancer, lymphomas, or chronic leukemias).

In Brief:

ASTRO Members Lobby Hill In First Advocacy Program

(Continued from page 1)

at OSI Pharmaceuticals in Melville, NY., was elected secretary. **Ruth Canty Gholz**, an oncology clinical nurse specialist at Cincinnati Veterans Affairs Medical Center of Ohio, and **Julie Painter,** a clinical nurse specialist/nurse practitioner at Community Health Network in Indianapolis, were elected directors-at-large. Members of the board continuing their service include **Diane Otte, Linda Abbott, Ryan Iwamoto, Patricia Buchsel, Ruth Van Gerpen**. . . . **ASCO** awarded 20 International Travel Grants to oncologists from 11 countries to help cover expenses associated with the annual meeting, June 5-8, in New Orleans. The awards represent approximately $125,000. . . . **AMERICAN SOCIETY for Therapeutic Radiology and Oncology** held its first legislative training and advocacy program in Washington, D.C., this week. During the two-day event, 35 ASTRO members from 19 states met with more than 70 U.S. senators, representatives, and congressional staff to promote legislative priorities, including increased funding for cancer research, enacting patient safety legislation, and correcting the Medicare Physician Fee Schedule. "Radiation oncology is an extremely important, but often overlooked specialty," said **Prabhakar Tripuraneni**, president-elect of ASTRO and a radiation oncologist at Scripps Clinic in La Jolla, Calif. "I think our members did an excellent job helping educate their congressional representatives and staff members about the critical role we play in caring for patients with cancer and other diseases.". . . **UNIVERSITY OF PITTSBURGH MEDICAL CENTER** and **Heritage Valley Health System** opened two ocations for the UPMC/HVHS Cancer Center, providing community-based cancer care at Beaver and Moon, Pa. Oncologists at both locations will work with more than 2,000 physicians, scientists, administrative staff and other health care professionals at UPMC Cancer Centers. Both sites will provide radiation oncology, cancer education and support services, imaging technology, and access to clinical trials in cancer prevention and treatment at UPMC Cancer Centers. "By collaborating with Heritage Valley Health System, cancer patients in this community will have improved access to therapeutic agents that target cancer and promising new treatment options," said **Ronald Herberman**, director of UPMC Cancer Centers and associate vice chancellor for cancer research, University of Pittsburgh.

Copying Policy for The Cancer Letter Interactive

The software that comes with your issue allows you to make a printout, intended for your own personal use. Because we cannot control what you do with the printout, we would like to remind you that routine cover-to-cover photocopying of The Cancer Letter Interactive is theft of intellectual property and is a crime under U.S. and international law.

Here are guidelines we advise our subscribers to follow regarding photocopying or distribution of the copyrighted material in The Cancer Letter Inc. publications in compliance with the U.S. Copyright Act:

What you can do:

--Route the printout of the newsletter to anyone in your office.

--Copy, on an occasional basis, a single story or article and send it to colleagues.

--Consider purchasing multiple subscriptions. Contact us for information on multiple subscription discounts.

What you can't do without prior permission:

--Make copies of an entire issue of the newsletter. The law forbids cover-to-cover photocopying.

--Routinely copy and distribute portions of the newsletter.

--Republish or repackage the contents of the newsletter.

We can provide reprints for nominal fees. If you have any questions or comments regarding photocopying, please contact Publisher Kirsten Boyd Goldberg, phone: 202-362-1809, email: kirsten@cancerletter.com

We welcome the opportunity to speak to you regarding your information needs.