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NCI To Suggest Changes In Cooperative Group Terms Of Award At Chairmen's Meeting Next Week

When the chairmen of the clinical cooperative groups meet next week, the Div. of Cancer Treatment will present them with proposals for changes in the "terms of award" which define the groups' relationship with NCI. Cancer Therapy Evaluation Program Director Michael Friedman emphasized that

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In Brief

Cech, Sharp, Dole, Weicker Receive 1988 Lasker Awards; Weicker Only Major Election Casualty

WINNERS of the 1988 Albert Lasker Medical Research Awards announced this week: **Thomas Cech**, Univ. of Colorado professor of chemistry and molecular and cellular biology; and **Phillip Sharp**, director of the MIT Cancer Research Center, shared the Basic Medical Research Award for their independent but related research on RNA. **Vincent Dole**, professor and senior physician emeritus at Rockefeller Univ., received the Clinical Medical Research Award for his work with methadone. **Sen. Lowell Weicker** (R-CN) received the Lasker Public Service Award. . . . **IRONICALLY**, Weicker was the only major casualty of last week's election, as far as the health and biomedical research constituency is concerned. His independence had attracted enough Democratic voters in the past to win three Senate terms in a state with a majority of registered Democrats. But too many Republicans came to consider him a maverick liberal and switched to Democrat Joseph Lieberman. As the ranking Republican and chairman of the Labor-HHS-Education Appropriations Subcommittee, Weicker gave powerful support to budget increases for NIH and NCI. His defeat, along with the retirement of Chairman Lawton Chiles (D-FL), removed the top two people from that key subcommittee. Republican membership on the Labor & Human Resources Committee, which has responsibility for NIH authorization bills, has been decimated. Orrin Hatch remains as the ranking minority member, but Robert Stafford retired, Weicker was defeated and Dan Quayle got another job. The Democratic lineup, including Chairman Edward Kennedy, remains intact. Key members of the House counterpart committees were all reelected. . . . **KEVIN SCANLON**, City of Hope biochemist, has received the Paul-Martini International Medical Research Prize for his discoveries of the mechanism by which certain cancer drugs kill tumor cells and why some tumor cells become resistant to chemotherapy.

Group Chairmen To Hear Proposals For Changes In Terms Of Award

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DCT had not determined the changes would be adopted as written and would be "discussed in great detail with the group chairmen."

DCT Director Bruce Chabner added that the changes "are simply proposals that we are considering now. They will be presented to the group chairmen for their comment and consideration." Chabner said they would also be discussed further with the DCT Board of Scientific Counselors before they are adopted.

Chabner, Friedman and former CTEP Director Robert Wittes have been talking with group chairmen about changes in the terms of award for the past year, as part of the ongoing discussions involving streamlining the groups, increasing patient accrual and other improvements in the system.

The chairmen, as with center directors and others whose grants are proscribed by NCI and NIH guidelines, have been a bit wary of changes. They generally agree that some are warranted, as long as they have a say in how they are written up.

The proposals, as presented by Friedman:

Protocol closure. "The Cancer Therapy Evaluation Program may well request closure for poor performance. This is something that we have not done very frequently in the past, but I think represents a very reasonable level of discipline in the system, if the results are already conclusive from other data, independent data, parallel data, the emergence of new information which makes this study less relevant. This is sensible, and you think it is self evident, but I think it is important to state. Of course, if there is some new information about patient safety, this could result in the early termination of a study.

"We will not provide investigational agents or allow expenditure of funds for a study after requesting closure, except for those patients who are already on the study, where it would not be justifiabile to withhold the medication.

"Early closure, that is prior to meeting the stated accrual goal in the protocol, should be something which is done only after the most careful sort of consultation. What we are asking for here is that the group or groups which wish to close a study early should please review that interim data with NCI biometry and medical staff to make sure that there is concurrence here.

"In the past, this has been done. On several occasions, it has been absolutely appropriate to close the study. We have been in complete agreement with it, and that has been very satisfactory.

"On other rare occasions, there have been disagreements. On one occasion, particularly, a study was kept open which, in retrospect, was probably quite properly kept open because important information was gained. What looked to be a disturbing trend did not hold out, and the study would have been terminated prematurely for not good reasons, basically."

Performance assessment. "What we mean by this is that the group needs to have in place a mechanism for not only assessing but supporting its members based upon performance. This will include some procedure for adjusting funding to individual members as appropriate for the level of participation in group activities.

"Here, we are talking about two different sorts of functions. One is patient accrual, the recruitment of patients onto studies. The second is the scientific participation in the intellectual life of the group.

"This could be of two different sorts. The first is some prospective system, reimbursing by the case, a capitation system, which some cooperative groups are very interested in pursuing, which we think has a lot of attractiveness because it ties very specifically funding to performance by accrual.

"But one could equally well defend a retrospective system, a financial adjustment being made at the end of the year, at the time of noncompeting renewal.

"We are not committed to one system or another. We simply think that given the real limitations that groups face in terms of finances, that they have to have some system of enforcing flexible changes within their own funding levels so that they can meet their own needs. This represents some sort of responsible management on their part that they would like, and we completely support this."

Strategy meetings. "One important thing we have been doing but we are now codifying is trying to hold strategy meetings to develop national research agendas. That is, the groups and cancer centers will be brought together to think about developing areas and how to prioritize ideas within those areas.

"Last year, we held a number of very useful and very successful meetings looking at colon cancer adjuvant therapy, rectal cancer

adjuvant therapy, hairy cell leukemia, chronic lymphocytic leukemia, breast cancer, melanoma, where there are more ideas than there are patients or resources, and how does one carefully and thoughtfully triage those.

"Obviously, there needs to be a consistent and ongoing dialogue between the groups and CTEP and at all points of protocol development."

Concept reviews. "Another new proposal we are making is that prior to the submission of a phase 3 protocol for review by CTEP, a concept review, a brief document describing the backgroud and the ideas, the goals of the research and the resources available for the research would be sent in for CTEP to review.

"This is completely analogous to the letter of intent system, which has been very successful for new agents. Before a group writes a protocol for a new agent, it sends in a letter of intent to express interest and willingness to perform a certain study in a certain way that is looked at. If it is approved, that group has that slot for that drug and that disease."

Protocol review. "This Board of Scientific Counselors has asked CTEP in the past, 'Why are we not more able to very carefully and with great rigor define the kinds of studies that we would like to see done?'

"One of the reasons for that is the amorphous nature of what was described in the terms of award for the protocol review process. This [change in the terms of award] attempts to be more precise about that. I don't think there are things here which are different than how we have functioned day to day for the last several years, but it is important to set this out clearly.

"We would like to require protocol review for all phase 3 studies, irrespective of the study size. The considerations which we think will be important for the approval of a protocol have to do with the strength of the scientific rationale supporting the study, the medical importance of the experimental question, the absence of unnecessary duplication--we are not talking about confirmation here; we are talking about duplication that adds nothing or adds very little; the adequacy of the study design--this is an area that a lot of attention is focused on; a satisfactory projected accrual period.

"Obviously, patient safety has to be a primary consideration, compliance with the federal regulations, adequacy of data management, appropriateness of patient selection, and workup and followup, and so forth. CTEP will continue to convey these comments in a consensus review. Disapproved protocols will not be conducted using NCI funds, and that is obviously sensible."

Data collection and management. "I include this to indicate that we are encouraging the simplest, most efficient ways of collecting and managing the data."

Quality control. "Obviously, very important. The timely medical review and assessment of patient data is extremely important, especially when we are dealing with phase 2 studies or early phase 2 studies when you need real time information on toxicities that are encountered, and you are able to adjust, not only to get more effective therapy but safer therapy. Collecting data every six or nine months is not satisfactory."

Annual reports. "There will be annual reports that we are asking from the groups, to include a lot of summary data dealing with performance by each member and each affiliate. This information is essential to us for not only analyzing the cooperative group program for the main members, the principal institutions, but also for the Cooperative Group Outreach Program and for other affiliate institutions as well. We have been asking for this information, at least some aspects of this information, more frequently to provide a better management of the clinical accrual rates."

Annual meetings. "We would like to propose an annual meeting with CTEP staff prior to the noncompetitive renewal time in order to critically review the progress of the group at that time. We think this would be a worthwhile yearly meeting to have to not only look at the past achievements and problems, but also to predict new areas that we should pay attention to."

Competitive renewal. "Given the budgetary picture that we are looking at, we think it is appropriate for the group to meet with CTEP to plan its application. This is frequently done anyway, but what will be added is that a budget proposal would be made. That is, a dollar figure will be identified for that group, which we think is reasonably likely, and the group can then structure its application based

on that dollar amount.

"Certainly, it is possible for the group to ask for more money. We are not telling you that that can't be done. But that additional money should be identified in sort of modular chunks, which are easily identifiable, so that the science of those modules can be reviewed, and the dollars associated with those modules can be easily identified. That is, if there should be more money available in the system and these other activities are well reviewed, we would then be happy to supply funding for it.

"If, in the worst case scenario, additional monies are not available, then the group will have already defined what the limits of its work scope will be, what its priorities are, and we will have some agreement ahead of time on that.

"I think this represents another reasonable management technique that we just haven't faced in the past because we haven't looked at the real difficulties of the funding system," Friedman said, concluding his presentation of the proposed terms of award changes.

Chabner said the proposals include "some significant changes. I think there is more involvement of NCI in some phases of protocol planning and also in the termination of studies. When we reviewed the group program last year with regard to accrual, the thing that was so noticeable was that there are many protocols that were just going nowhere. It would take them years to finish; they probably would never finish. We were limping along, with a few patients going on those studies.

Poor Accrual Reason To Close

"We think it is very important for good management purposes for us to have more of a voice in closing protocols. At the moment, the only reason we close protocols is because of safety or duplication. We think that just poor accrual is also a very important reason and also if the question is no longer important to answer."

Chabner said that if the group chairmen have any major disagreements with the proposals, they will be referred to the Board's Clinical Trials Committee. "We'll talk about it with you folks to try to refine what would be a reasonable position, and then bring the final package to the whole Board."

The cooperative group chairmen will meet Nov. 22 at NIH, Bldg 31 Conference Room 6, starting at 9 a.m.

Good/Bad News: Accrual Up Sharply, But Groups Get Little New Money

The clinical cooperative groups have been whacked over their collective heads (with the exception of the National Surgical Adjuvant Breast & Bowel Project and the Childrens Cancer Study Group) during the past three or four years by NCI and Div. of Cancer Treatment executives over the issue of patient accrual.

Former NCI Director Vincent DeVita went so far as to suggest that perhaps the groups should be abolished and some new system developed to carry out large scale phase 3 trials.

DCT Director Bruce Chabner, then CTEP Director Robert Wittes and then Clinical Investigations Branch Chief Michael Friedman disagreed, feeling that the group system has proven itself and that some refinements could lift accrual to satisfactory levels. They undertook efforts to do that, including establishing a program for high priority intergroup studies, payment per case, a nationwide publicity effort to sell clinical trials to the public and physicians, initiating fewer but better and more tightly focused protocols, decreasing the number of ineligible patients.

Charles Coltman, chairman of the Southwest Oncology Group and current president of the American Society of Clinical Oncology, dedicated his year as head of that organization to clinical trials participation. Other group chairmen undertook their own efforts to step up accrual.

CTEP estimated that the high priority trial/payment per case system would cost about $6 million a year. However, DCT was only able to come up with an extra $1.5 million above the $56 million already budgeted for the groups, and that was not available until just before the end of the fiscal year, in late September.

One might expect that all the rhetoric, new programs and good intentions would amount to little, given the poor financial support.

One would be wrong.

Friedman told the DCT Board of Scientific Counselors that during the past six months, patient accrual is up more than 20 percent for cooperative group phase 3 studies. "This has been at a time when there has not been dramatic new amounts of money infused to the system, so you can't say that this is tied to new dollars," Friedman said. "It does repre-

sent, I think, a real effort on the part of a lot of individuals to make this system more efficient and more effective."

During the same time period, the number of phase 3 studies had been reduced 13 to 14 percent. During the last quarter of the period, 13 studies were closed and five new ones opened.

Friedman said that four cooperative groups had recruited 157 new institutions or practices or clinics or hospitals into participation in their studies. "That is, institutions or practices that were not currently being paid by the group system. These are presumably new players, and the numbers of patients identified for the first half dozen trials that we wanted them to consider represented about 4,500 new patients each year.

Board member James Cox suggested that the groups might be encouraged to establish high priority trials "without necessarily thinking of requesting more funding. In other words, to identify them for broader participation in the groups with the expectation that the group will get secondary gain from it rather than money, and the same thing for enlisting the participation of cancer centers and CCOPs without additional funds, at least the cancer centers without additional funds."

"It gets to be a very tricky area," Friedman responded. "First of all, that has already been going on in a very subtle way, because there are fewer studies, and there has been more general agreement, not just by us. What this really represents is the groups getting together and deciding what they want to do and how they will share things. That has been very successful, especially in breast cancer and a number of areas where they have decided what they wish to do. Essentially, they have self selected what the higher priority trials are for them.

"Having a beauty contest where we designate certain things of high priority without dollar figures certainly could be considered, but unless that somehow were to permit something to be gained other than merely putting a patient on that designated trial, it is a little hard to see how that would stimulate new accruals.

"Getting cancer centers more involved and increasing CCOP involvement is an extremely important area," Friedman continued. "Many cancer centers do not participate adequately. They are very ingenious in doing early pilot studies and linking laboratory and clinical studies in a very creative way. . . Cancer center directors point to the fact that their core grants often don't have any funds at all for clinical activities, that they don't know how to fund such things, that they felt excluded from such decisions."

Board member Lawrence Einhorn said he was "very worried about the bladder studies, and I don't know how to fix it. I can tell you what happens at Indiana Univ., and it is probably similar around the country, where we have such poor accrual. The patient is initially seen by a community urologist, is referred to our university urologist for a cystectomy, period. The patient comes there thinking he is having a cystectomy, period. Our urologist and I explain the study. We have been able to get almost no one on that study [one of the five designated high priority trials currently under way, which compares cystectomy vs. cystectomy plus the combination M-VAC].

"I am wondering if we shouldn't send out a mini-clinical alert to the American Urological Assn. so that they are aware of this study, because they are. . . to a certain degree prejudicing the patients that are being sent [to the institutions doing the bladder cancer study]."

New SWOG Urology Unit

"You raised a number of really important questions," Friedman said. "I agree with you. The reason that bladder is included as one of the high priority trials is I was willing ahead of time to bet, as you are, that it is going to be a positive study. . . If it is worthwhile, then how do you get more patients on it? We are trying several different approaches. One is the SWOG urology component, which was recently reviewed and funded. This is a group of urologists, and the money is going directly to them, funneled through the Southwest Oncology Group office. One of the concerns that surgeons have raised is they don't have control of the funds [as does the new SWOG urological unit], they don't have the nurses and data managers to help manage the study. They didn't feel like they were in charge. . . We want to see whether this experiment will be successful. If SWOG's efforts are going to yield more patients more quickly, then this might be a model that we can use in other places.

"That is one experiment. Another is a very ambitious effort by the Office of Cancer Communications to try and not only educate health professionals as to the value of clinical trials but, more importantly, the general community population."

Survey Supports Clinical Alert, But Some NCAB Members Still Object

Reverberations from the clinical alert NCI sent to more than 13,000 physicians and others on the positive results from negative node breast cancer studies are continuing:

--Helene Brown told fellow National Cancer Advisory Board members that the Cancer Information Service office in Los Angeles which she heads had received calls from "literally dozens" of women treated over the last decade who "were alarmed" and wanted to know if they should go back in for chemotherapy.

--Editor Robert Wittes of the "Journal of the National Cancer Institute" summarized in an editorial the complaints about the alert: many physicians did not receive it; the contents were incomplete in that they referred to data that were not yet available; NCI has no business telling physicians how to practice medicine; and the alert bypassed the normal processess of peer review.

--In conversations with a host of physicians and others and in listening in on discussions about the issue, from the American Society of Clinical Oncology meeting in New Orleans shortly after the alert went out, through the summer and the fall NCAB and boards of scientif counselor meetings, **The Cancer Letter** did not hear a single person other than NCI staff members defend the alert.

And yet--

Shortly after the alert went out to the 13,000 physicians and cancer organizations whose names were obtained from the PDQ directory, NCI sent a followup mailing to 11,287 physicians who had received the alert; 5,465 responded to a questionnaire. The results:

* A majority (76.4 percent) responded favorably to the process NCI used to determine the need for an alert [the process included gaining approval of the NCAB, the PDQ Editorial Board, and the NCI Executive Committee]. Of those who did not find the process adequate, 33.7 percent suggested that NCI should wait to publish study results in a peer reviewed journal before issuing an alert.

* More than one half (59.8 percent) reported that the alert provided them with sufficient information for making a decision about node negative breast cancer treatment. Of those who said it had not affected their treatment practices, most either did not not routinely treat breast cancer patients or did not have any who qualified for adjuvant treatment.

"Apparently," one NCI staff member told **The Cancer Letter**, "we've only been hearing from those who objected to the alert. It's obvious that most physicians felt it was beneficial and the right thing to do."

Two surgeon members of the NCAB remained unconvinced. Samuel Wells and Walter Lawrence both had expressed reservations when then NCI Director Vincent DeVita and NCAB member Bernard Fisher had presented the node negative results and planned issuance of the clinical alert at the Board's May meeting.

"I think the main concern was that these data came out before they were published, and people were given advice on how to treat patients," Wells said at the recent NCAB meeting. "I think that in the future we ought to be careful about doing that. The clinical alert that precludes or predates any published information, peer review data, is where the fault lies."

"I misunderstood what we were doing as a Board," Lawrence said. "I expressed concern that it would be perceived by the public and by physicians as a directive from here on how to treat patients, and that PDQ would make it state of the art treatment. In fact, the alert was very accurate, as promised by Bruce Chabner, and I was sort of halfway reassured. But I didn't realize we as a Board were approving the action, nor did I feel like we were qualified to do that. I think this was a National Cancer Institute action.

"But subsequent to that, Bob in this editorial says that NCAB approved it. In the alert, they said we approved it. If we are going to be approving things like that, I am going to talk longer next time than I did last time, because I was very much against it.

"To my surprise," Lawrence continued, "it came out worse than I thought, when you think about it. Number one, the American Cancer Society felt trapped. They felt betrayed. They were trapped with this information they didn't known how to deal with, with the public calling in. The doctors in my area were sore as everything about it. I am surprised that 50 percent of the people who responded [to the questionnaire] sort of liked it, because that wasn't the response in our area. . . the American College of Surgeons separated themselves from the alert. PDQ went ahead as predicted and sort of made this state of the art, which I don't think it is.

"I think we should learn from this. I don't think we should be announcing big breakthroughs when they aren't really breakthroughs yet. I don't think we, as a Board, should be endorsing premature announcements.

"I think that the system will take care of it. The medical literature, the scientific community will decide whether new facts are worthwhile or not, and I don't think we should be doing it through this Board, nor do I think the National Cancer Institute should. . . We should believe in the peer review system for literature just like we believe in the peer review system for reviewing grants."

Div. of Cancer Treatment Director Bruce Chabner had this response:

"Helene talked about the problem of women who were treated years ago who did not have access to that information. There is a second group of people who really were the primary focus of consideration, and that was the women who had developed node negative breast cancer in the interval between the completion of the protocols, the termination of the studies, and the publication. The prediction was that it would take months to get this into print and, in fact, it has happened that way.

"In the intervening four or five months, thousands of women with this presentation have been treated. The decision had to be made about whether these women should have the opportunity to be treated with adjuvant therapy. I think this was the most important consideration in the minds of the people who initiated this.

"It is true," Chabner continued, "that this wasn't published, but the protocols had been closed, after careful review, because of their positive nature. The material was reviewed within the Institute. I think, when it was presented to the NCAB, the intention was to get the endorsement of the NCAB.

"It is important that when the alert was sent out, no endorsement of treatment was made. It was simply stated that we feel that this information should be available. I am very supportive of the idea that a broader circulation should have been made. I think omitting the surgeons was an error because they see most of these patients. I think the primary decision that was made was whether this information should be made available prior to publication because of its public health impact. The number of women [diagnosed with node negative breast cancer] in the four to five month interval between closing of the protocols and publication would have been something like 15,000 to 20,000. I think that is a significant number.

"You can take the alternative point of view and say that we should simply wait for publication, and that that is more important than considering the potential impact on these people who could use the therapy. I want to emphasize, though, that the alert did not say every woman must be treated; it simply said that this new information is now available and should be considered by physicians who are presented with patients like this."

"Not all scientific judgment at the present time states that this has improved therapy," Lawrence responded. "So to say that you are withholding treatment for 15,000 to 20,000 people because they didn't have the hot poop in their newspaper yet is really not fair."

"I think you are right," Chabner said. "We don't know how beneficial it is going to be. All we can say is that there is an improvement in disease free survival. The down side , certainly of tamoxifen [one of the agents in the study], is small. There is reason to believe that it will be beneficial because, in most instances, disease free survival ultimately translates into survival."

Chairman David Korn suggested that a mechanism might be worked out with one or more of the appropriate journals for rapid, peer reviewed publication of results in similar future cases.

President's Cancer Panel member William Longmire suggested that an emergency consensus conference could be considered, and Chabner agreed.

"I believe we could have a consensus conference, but I would caution there is absolutely no substitute for peer review research in publication," Wells insisted. "I think that until that is done, all we have to do is make one mistake on one of these clinical alerts and school is out. I think we ought to get the data published in an expeditious way, let people read it, and let the chips fall where they may."

Ex-Officio Board member Dorothy Canter observed that "thought should be given to what you tell women who were treated two years ago, or five or 10 years ago. When they read something like this, it increases their anxiety about their own situation."

NCI Deputy Director Maryann Roper is not one to stand on the sidelines when a controversy is raging. "I have gone through this meeting being entirely too agreeable and it is time for me to be inflammatory," she

said. "There was one comment I heard Dr. Lawrence make that I disagree with.

"The clinical alert wasn't really my idea. I wish it was. I think the concept of a clinical alert is a good idea, and I hope we repeat it. I think an intent, maybe not a major intent, of the clinical alert was to approach the problem of the publication gap. Everyone has alluded to peer review, and that is ultimately the most desirable thing. But I think the realities of the publication gap are also a very real thing, an undesirable thing.

"Dr. Lawrence said he didn't think it was the role of NCI to do things like this. I disagree with that. I think it is the role of NCI to twitch the system. If this is one way of twitching the system that can accomplish something, then I think that would be very helpful. I think it is the role of NCI, that when we know something that could potentially benefit people, it is fair for them to know it, too. If I know a phase 2 agent works and therefore I can get my friends and relatives on those studies to hopefully make them benefit, it is fair for you to know that that phase 2 agent works. It is kind of like insider trading."

Wittes, who is serving as DCT deputy director in addition to editor of "JNCI" pending his departure for Bristol-Myers next month, said he agreed with what Chabner had said "wall to wall. Much of the tenor of the discussion here is the discomfort to the medical community that the alert has engendered. I think some of that has been procedural, and I tried to point out [in his editorial] ways in which we could have done better.

"But it has also been a conceptual problem to a lot of people, and I think that is wrong. I think that when data related to treatment becomes available, then it belongs in the public domain as quickly as possible. We have a failing, you know, that a lot of journals simply don't regard expediting the peer review process as a priority matter, and they should.

"We have a mechanism here that does that ["JNCI"]. We could have had these papers peer reviewed and back to the authors six weeks from inception. We probably would have done it shorter than that in view of what we perceived to be the urgency of these results. The journal now is set up to publish accepted manuscripts within about six to eight weeks of the receipt of the final one. So the mechanisms exist. People have to use them.

"I think that the experience that the NSABP had with its BO6 trial [lumpectomy vs. total mastectomy, when the "New England Journal" held the manuscript for nearly two years before publishing it], and how long that took in review, there has never been any satisfactory explanation, made public at least, why it took such a long time. But that was a situation in which a lot of people found the results, if not unbelievable, at least discomforting also. I don't know what role that had in the long delay of that manuscript.

"There was a lot of public flack about that," Wittes continued, "the notion that tax money was being used to generate data of concern to a very large number of people in this country. The peer review system itself had massive lesions in it that were preventing rapid dissemination of the results.

"It is okay for all of you folks to sit around the table and say things should happen fast and the peer review system should be fixed and figure out some way to fix it, but the Cancer Institute doesn't control the peer review system. We do what we can do.

"In retrospect, even with the warts and the mistakes that we have made, I feel completely comfortable with what we did, and, frankly, I would do it again. Given the appearance of important results, I would do it again."

Chabner later discussed the issue with the DCT Board of Scientific Counselors.

BSC member Charles Balch said he disagreed with the contention that the press had caused most of the problems by misinterpreting the alert. "Language in the alert was confusing. Patients in the trials were high risk node negative. It is not fair to say now that all patients will benefit."

Chabner acknowledged that patients considered good risk, that is, those with tumors small than one centimeter, had been excluded. But he insisted that "most of the information you would want in a publication was there."

Balch agreed that the "clinical alert may be appropriate and necessary in the future. I just ask that the DCT Board of Scientific Counselors be involved." Chabner said it would.

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