

CENTER FOR MIND-BODY MEDICINE  
COMPREHENSIVE CANCER CARE 2001

CONCURRENT: NCI Best Case Series

Arlington, Virginia  
Saturday, October 20, 2001

SPEAKERS: JEFFERY WHITE, M.D. National Cancer Institute; COLEEN LEE, RN, MS,  
AOCN National Cancer Institute

P R O C E E D I N G S

DR. WHITE: Thank you for coming. I'm Jeff White. I'm the Director of the NCI's Office of Cancer Complimentary and Alternative Medicine. I'm an M.D. I'm a medical oncologist, hematologist. I've been at the Cancer Institute for about 11 years now. But back in 1998 the NCI developed this office and the goal of it was to try to allow the NCI to have a prospective agenda in complementary and alternative medicine. I'll give you just a little history before we go into this particular session just to give you some orientation to what we're talking about. But let me ask. We've actually talked about Best Case Series at this conference for three years, I guess. This is the third year. We didn't do it in the first year. Was anyone at any of the previous talks that I gave about Best Case Series? That's right, I remember. Okay. So, thanks for coming back, and I guess you've heard some of this preamble, but I'll give it again for the people that don't know that much about our office. So, we got established about three years ago, and one of the major functions of ours, we have -- and there's another session that goes on that talks about funding CAM research, and our office does fund -- the NCI certainly does fund CAM research and, as you know, the NCCAM funds it, and these are important sources, but we are also trying to identify and bring to your attention other groups that do fund research and perhaps will fund the kinds of innovative work that CAM practitioners and CAM researchers want to do. So, I'd encourage you to go to that session as well. But I'm not going to talk much about funding of research programs today. What I want to talk about is another program we have, which is called our Practice Assessment program. What the goal there is, is to have more direct interaction with the CAM practice community, and we're trying to develop this interaction around data, okay, around specific documentation of CAM modalities used to treat cancer for which people feel they're effective, and we have two basic approaches to that. One is a retrospective approach, which is the Best Case Series. That's the one I'm going to talk about. Another is a prospective approach, which we are calling the -- and we'll get to that in a little bit -- either prospective outcomes monitoring or practice outcomes monitoring. I'll mention that. But we really want to talk about the Best Case Series today. So, the goal of this, as I said, is to try to develop a dialog around actual data, and so what we're looking to do, then is to provide an independent evaluation of retrospective data obtained from practitioners who adopt alternative medicine approaches to treat cancer. So, when I say "independent" ....what the role of that, what the outcome of that is .....so what we want to do is to bridge some gaps. I mean, I think probably most people would say that there are gaps between the conventional medical community and the CAM medical community and the conventional research community. And this is our attempt to try to bridge some of these gaps so that we can develop a dialog and push forward ideas that merit further

investigation. So, what's the history of this program? Well, what we're looking for is -- originally we conceived the program -- the program actually goes from 1991 -- I guess it was on the other slide, the next slide to come -- and it was really conceived of as a national program. However, it has quickly caught on. Well, let's put it this way. There has developed a certain international interest in the program, and perhaps to a greater degree than in the United States in some areas. So, one of the very first submissions that we've had since I came to this office was from India. So, although our focus is really to try to look at American CAM therapies, because I think the follow-up of those interventions is going to be easier -- taking something -- gathering more perspective data about an intervention like that is probably logistically easier than dealing with something in China or India or the Philippines or something like that. We are open to looking at anything that comes to us from any venue. Submission of anecdotal data to the NCI is really what we're looking for, but groups of this data -- not -- this program is really not designed to look at independent case reports that patients give us. It does not mean that we're not interested in independent patients' experiences with the treatment of CAM interventions, but what we're trying to do is to gather at least enough data that would be convincing to independent review or review board that would make recommendations about taking this forward to further investigation. There are very few individual cases that I think would do that. I mean, certainly if someone has advanced metastatic pancreatic cancer and treats it with an alternative approach and receives absolutely no other therapy and the tumor goes away completely and they live 5, 10 years after that, anybody's interested in that case, you know. But that's not the average kind of case that you're going to get, so if you try to make decisions -- and we're going to look at some of the kinds of cases that we might see and try to determine what would be good cases, what would be cases that perhaps are not that persuasive. Requests for additional data supporting a CAM approach. Let's go a little past this slide into the more specifics about the history. I think some of you know about the Office of Technology Assessment Report in 1990 that looked at unconventional therapies of cancer. Embedded within that report were some comments about looking at case report data, and there was a large experience that the NCI had in looking at data from certain specific CAM interventions, like laetrile that I think informed those recommendations. The recommendation was that the NCI should have a systemized approach to looking at case report data. So in 1991 that was established. It's called the Best Case Series Program, and it went on for several years, I think without a lot of advertisement. I don't believe too many people really knew of its existence, and there were not very many submissions to it. I'll tell you about some of the submissions that came through. But in '98 our office came about. We were more focused on this area, we tried to put more energy into examining these cases or getting submissions to these cases, and in 1999 we added an external review. Up until that point, really, all of the data had been looked at within the NCI, and there wasn't a board of independent investigators that would make an assessment of the value of that information, so in 1999 the Cancer Advisory Panel for Complementary and Alternative Medicine was established. It's a chartered panel of the National Center for Complementary and Alternative Medicine, and it is comprised of both complementary and alternative medicine practitioners and conventional researchers, cancer researchers. I'm going to go through this quickly just to give you a sense of what happened in the early years of the Best Case Series, and I'm not going to talk specifically about these interventions because really the goal is to talk about where we are and where we're going. There were, in this period, only 10 -- in seven years there were only 10 inquiries or requests for review of materials about best cases of these different therapies. What that generated was -- conducted reviews, so of those 10, four of those didn't go onto actually accumulate any

data at all. They were mostly just contacts, and six of them generated some information that warranted either further follow-up, requests for more information, or an attempt to try to gather sufficient information to make recommendations. And those are the six that are identified there. To actually get cases that had enough material that could be audited -- which means that you could actually look at the pathology slides, actually look at the radiographic films for those six -- had enough data to do that, and those are the ones listed there. So, you can see that there was relatively low activity, but what generated out of it was four projects. Two of them were NCI-supported clinical trials -- one of angioplastins, one of imagery therapy. Independently supported trials -- recommendations went back to the practitioners to do prospective evaluations in these other two approaches -- the Kelly regimen, which I think some of you may know as the Gonzalez regimen -- and shark cartilage. That's just a little of the background, so I want to introduce you to Colleen Lee, who has just recently actually joined our office and who is taking over the day-to-day activities of the Best Case Series program and the Practice Assessment program. She's a very experienced oncology nurse with a research background at the NIH for several years, and what she's going to talk to you about is really the process of this partnership that's developed in the evaluation of the Best Case Series program and where it's led us today, and then we'll flip back to me at some point to talk about really what the issues are now. And at that point, I'm going to save -- I'm going to try to keep track of our time pretty closely so that we can save a good, at least half hour to dialog about this. I mean, because really I want -- that's the biggest role that you can do to help us, is just to frankly talk to us about the program; what things might -- what things we could do to improve it, to make it more directly applicable to your situations; how we could encourage -- how we could get the word out to other people about this program and encourage submissions to the Best Case Series. So, Colleen, why don't you pick it up.

MS. LEE: I want to talk a little bit about the close relationship between the OCCAM, from which we're from, and the NCI. I didn't realize how large and broad spreading the NCI was, even though I worked within the Clinical Center for over 14 years, not realizing it's broadness, as well as its integration in many areas. And I actually did a little bit of research on the NIH, which I would like to share, in particular, in looking at the relationship between these two areas. The NCI is committed to finding innovative and promising therapies for people with cancer, and that we know. It's one of the largest institutes of the NIH, and it's organized into the Office of the Director. There's one Center, and it has six divisions, and each is separated into a different aspect of cancer research. The Officer of Cancer Complementary and Alternative Medicine is one of those offices, and it falls under the Extramural Branch, and the director of that office is Dr. White. The OCCAM was established in October of '98, as he mentioned earlier, and it has a couple of major responsibilities. It facilitates the development of the agenda, and we talked about that a little bit before, the perspective agenda for NCI and its close relationship with CAM research, and it coordinates the NCI's collaboration, and it mainly is in support of developing high-quality research and it provides an interface with the public. The NCCAM, as you know, is the National Center for CAM and is one of over 20 institutes and centers composing the NIH. The NIH is one of eight health agencies within the Public Health Service of the U.S. Department of Health and Human Services. In 1998 Congress established the NCCAM to replace the Office of Alternative Medicine, and its mission, as you know, is to simulate and develop and support research on CAM across several different diseases and conditions, all for the benefit of the public. NCCAM is an advocate for quality science and rigorous and relative research and is open to objective inquiry in which CAM practices are effective. It's overriding mission is to give the

public reliable information and safety and effectiveness, and that's why we're all here. CAPCAM, Cancer Advisory Panel for Complementary Alternative Medicine is an unbiased -- and that's one thing we'd like to put forth clearly -- unbiased panel of experts in both conventional and cancer therapies. I was a little interested more in who exactly made up the CAPCAM. It's a 15-member panel, and it's composed of mainly medical and surgical oncologists, an oncology nurse, CAM specialists, a statistician, epidemiologists, a patient advocate, and a radiologist, among others. And practitioners who have developed case studies that have been reviewed in the Best Case Series and deemed acceptable may have their cases presented before this panel. This brings us up to the present day Best Case Series program, which I'm calling the Millennium. I've divided the process of the Best Case Series into four tiers in this pyramid from tier 1 at the top at it progresses downward to the bottom to tier 4. The first tier is CAM use and community practice. The second is case study development and then submission for a best case series review. The third tier is a Best Case Series case study review and then request for additional data. The fourth tier is case study presentation to the CAPCAM and possible POMES initiation. We're going to take a look at each one of these tiers individually. The first tier is the use of alternative medicine approach and community practice. It is your present day practice -- the focus is generally on the approach -- to treat one or more cancers as a solitary intervention or combination therapy. The tumor burden is measured at various intervals, as well as the overall response to therapy, and that could be the tolerance of the intervention, the quality of life as symptom management. Tier 2 is case study development and submission for Best Case Series review. Generally speaking, when practitioners develop their successful cases into a case study, the focus remains on the approach and how the approach brought about tumor regression. Critical areas of focus -- as case studies are developed from our perspective -- several different areas. The first one is a definitive diagnosis. Send us a copy of the pathology report and operative report for each surgery, as well as official documents supporting the staging or grading of the tumor or tumors. The second area of focus is on a measurable tumor. If you're treating a primary tumor or tumor with metastases, send official documentation regarding the tumor's measurements over time -- for example, through a CT or an MRI. If the tumor type has markers associated with it, such as CA125 for ovarian cancer, send us laboratory reports with these values over time. The third area of focus is the alternative approach itself. Ideally, to best differentiate whether tumor regression occurred as a direct result of your intervention, your intervention must be given in isolation of any other standard therapy with a margin of time between the end of therapy and the beginning of your intervention. For example, if a patient received standard treatment of surgery-radiation-chemotherapy, and your intervention was introduced, it would be ideal if there's a time span between the end of your standard therapy and the beginning of the alternative approach, the reason being how can you firmly assert that your intervention resulted in tumor regression when the chemotherapy and radiation may not have had sufficient time to work.

SPEAKER: ----- sufficient time?

DR. WHITE: There's a little standard within the world of clinical research. When you're bringing patients onto the clinical trials and they've had prior therapies, in general you ask that they have been without chemotherapy or radiation therapy intervention in four to six weeks. Most of the time it's four weeks. It really depends on what the intervention is, and sometimes it does get stretched out to six weeks. That's the ball park.

MS. LEE: This leads us to the fourth area of focus, evidence of tumor regression. Using the example I just referred to, it would be ideal if diagnostic tests were obtained at the end of standard therapy showing the status of the disease just prior to the initiation of your intervention. This timing is optimal in order to validate your assertion. If diagnostic tests are not performed after standard therapy to show disease status before your intervention is introduced, then how will we know to what degree tumor regression occurred as a result of your alternative approach? It goes without saying that the development of effective cancer therapies requires uncompromised standards of evidence, and evaluation of CAM research is no exception. We have a sample case study format that's available on our website. This is the beginning of what it looks like. You can either download it from the website or we can email it to you, send to you as an attachment. And the address is there on the screen, and it's also on your outline. It goes through five main areas: Clinical history, prior therapies, treatment descriptions, response to the intervention, and any toxicity during the treatment. When you're at a point of pulling together all of your data for case study, call us, and we'd be happy to talk it over with you. For the initial round, we're looking to be sent paper copies of either the pathology slides or diagnostic studies. Down the road we will ask for the slides. This will be the first initial round. This leads us to tier 3. After we receive your case study submission, our review process begins. Our focus is non-biased and is on the process itself versus the alternative approach. There are some questions that will be posed to each case study. Is there a definitive diagnosis? And added to that, what is the stage of the disease? Is there a measurable tumor? And how is it measured? Are the measurements used the ones typically used to devalue this disease? How was the disease initially treated, and are they considered standard therapy? Are there concurrent therapies? Is there evidence of tumor regression or remission? Are the appropriate diagnostic reports included in the case study, and are more reports necessary to understand the progression or regression of the tumor? Most case study submissions require additional reports, so this is an area of focus for you as you assemble your data. Dr. White and I will carefully review each case for scientific merit and gaps in information. We'll go ahead and prioritize the case submissions based on our preset criteria and provide you with a summary of our findings. We may request to speak with the treating physician or perhaps the patients themselves. The next step after all outstanding reports have been submitted and reviewed, we will ask for the pathology slides and actual films, which will then be reviewed by experts at the NIH Clinical Center. Tier 4, case study presentation to CAPCAM and possible POMES initiation. You'll be scheduled for the next CAPCAM meeting in the Washington area. Of all your cases submitted, the best four or five will be presented. Either you, your designee, or one of us can present your cases for you, and this is your choice. Travel and accommodations for practitioners presenting a Best Case Series will be paid for by the NCI. CAPCAM meets on an as-needed basis, so at this time there are no regularly scheduled meetings. The focus of the panel is the scientific merit of your intervention and its ability to bring about tumor regression and complete remission. If your approach shows solid evidence of effectiveness, it may be studied further with the support of the NCI and/or NCCAM through a POMES design -- perspective or practice outcomes, monitoring, and evaluation study. The POMES program provides the resources necessary to implement small, perspective, observational studies of patients treated in CAM practice settings, and generally this is less than 50 patients. And this can occur in various parts of the country or the world. So, this leads us to a very, very important question that I know is in the back of your mind: What constitutes an awesome case study? And the converse of that: What constitutes a not-so-awesome case study? Mean qualities of an awesome case study: Definitive diagnosis, measurable tumor, no concurrent

therapy ideally, and evidence of tumor regression. We've developed a hypothetical case study that we want to go through and let all of us think a little bit about where this individual is and how this case is presented and what are some of its merits. Ms. Candace Barr is a 45-year-old woman diagnosed with stage 4 epithelial ovarian cancer during a staging laparotomy with tumor debulking in January 2000. A preop abdominal CT scan showed metastatic spread to the ----- and small intestine. Preop chest CT and bone scan were negative. CA125 was 300. The pathology report indicated clear margins. She completed four cycles of chemotherapy. The restaging CT showed residual disease, and that was June of 2000. CA125 was 300. She decided against further standard therapy. She began an alternative approach three weeks following her restaging. CT scans in November 2000, March 2001, and October 2001 showed no evidence of disease. Her CA125 is now 35. First area we want to look at: Is there a definitive diagnosis? What do you think?

SPEAKER: Yes.

SPEAKER: Yes -----

MS. LEE: Indeed.

DR. WHITE: There's a caveat to that one, but I think this is a good case, and there's a little -- I'll throw a little wrinkle into it. Let's say the patient had this well-diagnosed ovarian cancer and underwent all this therapy and went into a complete remission -- I want to change it just briefly just raise a point -- and then had a recurrent lesion that was seen on a CT scan. At that point -- let's say that we didn't have a marker -- let's say we didn't have a CA125 to go by and all we had was a recurrent mass, and then she undergoes some therapy, some alternative therapy and the mass is no longer seen on CT scan. All right, now what is that case? Is that recurrent ovarian cancer, or what? So, is that diagnosis well made? I think -- that's a case that you have to say, well, if you've got other cases, that one is going to be in the kind of suboptimal range. I just want to raise that because we run into those kinds of situations. Because this patient wasn't ----- right? She had disease at the beginning. She went through therapy. She didn't go into a complete remission and so this lesion that's seen on CT scan is assumed to be -- and we have a marker that says that she still has disease, so more than likely that lesion is disease but we didn't biopsy to know that it's disease. So the only point is that initial diagnosis of cancer doesn't mean that you've got cancer at some later point at which you start another therapy.

SPEAKER: You're saying the second ----- is not an adequate diagnosis for you?

DR. WHITE: No, no. No, no, I'm actually changing the case. What I'm saying is -- and the reason I'm -- because we only have one or two cases so I'm trying to elaborate on some of the cases to give you a feel for situations that are a little than clear. So, a situation in which -- this patient didn't have a second-look laparotomy, just had a CT scan. Oh, you know what? You've got a different thing from what we've got. We changed it -- we changed the --

MS. LEE: We changed the line of treatment overnight.

DR. WHITE: Yes, actually we changed the slides from what you have. Okay. But the bottom line is I'm really not saying that this is not a valuable case. Well, we had a humorous one that we put in there but we didn't leave it in. This isn't a valuable case. Definitely. I'm not conflicting. I'm not trying to confuse you about that. I'm just trying to extend the dialog about other cases. Let's keep going.

MS. LEE: Okay, she has a measurable tumor. Preop abdominal CT showed metastatic spread to the omentum and small intestine, and then her further workup showed a negative chest CT and bone scan and she had a CA125 of 300, and the pathology report indicated clear margins. And then following, she had a restaging CT or the second ----- it showed residual disease, and that was six months after the initial presentation, and her CA125 was still 300. So, there's something to measure. She had no concurrent therapy. She began standard treatment with four cycles of chemo. She decided against further treatment. She began alternative therapy three weeks following her restaging. So, there was a gap of time in there. And she also had evidence of tumor regression. CT scan following. Subsequent one showed no evidence of disease, and also the marker that was used to follow her initially is now down to 35, within the normal range. Do you want to add anything before we go on?

DR. WHITE: No.

MS. LEE: Okay. So, in contrast, some of the areas that make determining whether a case study is acceptable or suboptimal usually revolve around these areas: Around the diagnosis, ability to measure the tumor, concurrent therapy, tumor regression or remission, and documents to support the case. So, we're going to take a look at another case study, and try to look at this as if we didn't go through the first one. Here's Ms. Candace Barr. She's a 45-year-old woman diagnosed with ovarian cancer January 2000. A preop abdominal CT scan showed metastatic spread to the omentum and small intestine. Preop chest CT and bone scan were negative, and she completed chemotherapy A. Restaging CT scan revealed new abdominal disease in June, six months after, and she received chemotherapy B, along with alternative approach three weeks following her restaging. CT scans in November 2000 and subsequently showed no evidence of disease. MS. LEE: So, taking a look at her diagnosis, is it definitive? If this is all one has to work with, would you call that a definitive diagnosis? What it could have is perhaps the stage of a disease or perhaps a cellular type that would put things more in context. Is there measurable tumor? Is there enough information at the presentation of the second case study to say that it's being measured consistently with perhaps one or more means, something that can be followed? A preop abdominal CT showed metastatic spread and preop chest CT and bone scan were negative, so there wasn't any other disease. We don't know how much original bulky disease she had. So, that would be helpful because over time we would want to be able to go back. You assume that part of that was resected but it's uncertain as to how much disease was remaining after the initial surgery. And it said a CT scan revealed new abdominal disease in June six months later. So, you kind of want to ask the question, first of all, did she have a CA125 prior to surgery? Did she have a CA125 six months later? Are there comparisons between the two? When she was restaged six months later, did they repeat the chest CT and bone scan? Did she have any further evidence of disease beyond her abdomen? So, those are some kinds of information that can be included to make it an awesome case study. A challenging area that we look at is the use of concurrent therapy. And you've heard me mention with emphasis ideally there could be a gap of time

between when standard therapy ends and when alternative therapy begins. This particular person completed chemotherapy A. She received chemotherapy B, along with alternative medicine three weeks following her restaging. One of the things that we would want to know is what kind of chemotherapy did she receive? It begs the question how do we know how effective the alternative therapy can be if it's given alongside other interventions, and that's a difficult question to answer. And the final area that we took a look at is tumor regression, or remission. A preop abdominal CT scan showed metastatic spread to the omentum and small intestine. Restaging CT showed new abdominal disease and then down the road showed no evidence of disease. What's missing here falls into the amount of tumor measured that we discussed previously. It's terrific to see that there's no evidence of disease but it's difficult to note exactly how much disease was there to begin with. So, it makes the case of tumor regression or remission stronger if you know how much original disease there was. And are awesome case studies possible? The answer's yes, and that's why we're here. And what can we do to help you? And that's what we want to know. Okay, that's me on the left and that's Dr. White on the right. What we can assist you with is guidance in many different areas. We can help you with case selection. We can also help you with prioritizing because it takes a lot of effort to put together a case study, and if you want to speak with us ahead of time, we can help you prioritize which ones you should put your efforts and focus into. Also, obtaining copies of reports can be difficult, so we ask that you make every attempt to try to do that. If you reach some roadblocks, we can assist. We can make phone calls, let people know that this is important and what the ultimate goal is. We can try to do that to help you. Also, myself being to new this office is not as knowledgeable as Dr. White is about all the resources that are available and the entire CAM community, so for questions such as that, being connected with somebody who has either developed a case study prior or who has worked with a particular alternative therapy that you have experience with, we can assist you in doing that. DR. WHITE: All right, and a couple more slides, then we're going to open up to start a dialog. I'm going to skip this because it will come out in the other slides and discussion. So, really what we are asking for you is to identify the cases that you think fit these kinds of criteria, so there is that first screen that you need to do, that you need to identify these cases, and what we recommend that you do is to actually look at a little case history of it and see if it fits these kinds of criteria that we're talking about. Do you have a definite diagnosis? Do you have clear evidence of a remission that's radiographically documented. This is talking about predominantly solid tumors. There are other tumors you don't even talk about. Is that information there? Was there any concurrent, conventional therapy? So, that's the screen that you do in your mind to try to identify a case that you think -- okay, well, I think this is an invaluable case. All right, and then if you have -- even if you have one of those -- I mean, I -- the Best Case Series is really a series. I mean, what we're looking for is several cases. And the CAPCAM, as Colleen mentioned -- we're looking for presentations of at least four or five cases. All right, so to get to that stage, you need that volume of material. However, if you think that you have some hugely interesting single case, we'd certainly be interested in talking to you about that. All right, so, contact us -- I want to get that across. Rather than put together a bunch of cases and then put them in the mail and wait for a response, give us a call or email us or something. Talk to us. And let's discuss what it is that you want to do. And if you have some of these vignettes of cases in your mind, I mean, it's just written out briefly and you want to talk about -- I mean, I think I have 15 or 20 of these. How should I prioritize these? I mean, we can give you sort of a sense of which of those you ought to focus on because I can see that it certainly would be frustrating that you start off and you pull together three or four cases and get everything together for those, submit the information, and

then we tell you that none of those really are the optimal cases. All the work that you put into it and so now you're sort of turned off from the process. So, get in touch with us early so that we can perhaps help you focus your energy and time. So, I can't emphasize that enough. Summarize the history. I say do that for us as well as for you. Sometimes we get submissions that are just reports, pages of reports, and that's it, and there's no discussion about what happened to the patient, if they got any other concurrent therapy. Sometimes you can't read the handwriting, you know, so the easier you make it for us, the better, obviously. But also I think it helps you if you think through the process, think through the case. You look for the pieces, and if you say, well, you can't find that piece, well, then you can move onto another case. Obtain consent for a document release. Well, this is important because what we're looking for is really the actual pathology slides and the actual radiographic films. This material is really the patient's material, and if they for some reason don't want that material reviewed, then -- I mean, that's their prerogative. So, it is useful -- I mean, it is imperative, I guess, that you let the patient know what you're doing with their own materials. Gather necessary documents so you pull it together in some kind of a format that's easy to follow, and submit them to us. We can even help you with the mailing issues, with taking care of the postage and that kind of thing, particularly when we get to the pathology slides and the radiographic film, which could be the bulk of material that you're submitting. Okay, so how do we try to get this message out about the Best Case Series? Well, this is one form that -- we've done that for three years now, talk about it at this conference. You know, I think we penetrate a group of people that are serious and interested in this approach and we get some response from that. But what we've also done is some advertisements, and I don't know if any of you have seen them in some of the journals that we've put them in -- I'll let you know what journals they're in; direct mailings -- letters that we've directly sent to people that we think might be doing this kind of work, treating cancer patients with alternative interventions; these conference presentations. Our own website has information about the Best Case Series program that you can download, as Colleen was saying. -- which is a lay magazine. Alternative therapy is ----- Medicine, Clinical Practice of Alternative Medicine focus on alternative and complementary therapies, which is actually a UK journal or ----- journal. The Journal of Alternative and Complementary Medicine -- people call it the blue journal; Townsend letters. So, one of the things I want to ask is, you know -- so, now we're in the dialog section, so as much input as you can give us we would appreciate it. So, journal names are fine, but the approach that we're taking I'd like some comments about it. I mean, if there are professional organizations that we ought to go to -- to get to your colleagues, to talk to them about this program -- then, please let us know what you think are the most relevant ones that would have people treating cancer patients with alternative approaches that we can talk to. If there are other journals that we ought to be doing, if there are people that you think we ought to directly contact, and if you don't want to give out names right now, then if you can get to me afterward. So, I'd like to know if you think that people know -- how many people, before you came to the conference, knew about the Best Case Series, for example? All right, so maybe, I don't know, a third or so. Are these -- how many practitioners are here actually who treat cancer patients? Okay. Are these the places that you -- things that you read or -- what are we missing? How can we get to you or your counterpart in some other city or town or whatever?

SPEAKER: I'm a dietician and I think what I would want you to do ----- and there are certainly -- you know, not everyone in it by far practices ----- therapies, but there is very large

----- number, particular the newer generation has ----- that's one ----- the other things I thought of that are popular, like the Yoga Journal is another popular well-read journal.

DR. WHITE: Okay, thanks. We'll certainly look at doing that. Yes.

SPEAKER: Are you looking at ----- one alternative -----

DR. WHITE: Yes, actually I should have given just a general opportunity for questions and answers rather than launch into this, but, yes, it's not necessary that the intervention be a single herb or something like that. It can be a complex regimen. If you are treating patients that are being treated by other physicians with alternative approaches as well, then that does not mean that there's no way that we can look at that. But you can see that it would make it complex, that if you're giving, for example, some dietary intervention and the patient also receive -- and we certainly had cases like this -- the patients receive from somebody else an herbal intervention, but -- and, actually, the person that submitted the -- actually, it was two herbal interventions -- the person that submitted the information about the one herbal intervention was making the claim that this was in response to their intervention. But they actually were aware that the patient was on another herbal therapy as well but, I guess, just didn't believe that that was an effective therapy. But, I think if you were a impartial observer on a panel who was looking at a case like that, you would not be able to make an assessment. Now, if this patient had advanced metastatic disease, as I said, went into a complete remission, you don't really care which of those interventions did it, as long as you have it well documented that it was both of them. That gives you at least a justification to do some research into the combination of those things. So, no, it doesn't matter that -- it doesn't have to be a single intervention, but what we are looking for is really complete documentation of what the patient received so that we don't end up going down one road, studying one of those herbs -- which was the ineffective one perhaps -- just because we weren't aware that the patient happened to be on something else. John?

SPEAKER: If you're collecting case studies prospectively, do you need informed consent or IRB approval?

DR. WHITE: Yes, we are taking that approach that if we are going to be following patients but -- the reason we're doing that is that we're going to be -- well, I don't know that you have to do it is my answer, and that's the approach that we're taking. And I think there are ethical reasons that we are doing it and certainly NIH kind of policy reasons that we're doing it, so if you're not in that environment, is it a research protocol? I would say it is. Even if it's -- I guess if you went to an IRB chairman and asked him that question, which I would do, or the Office of -- what do they call it now? It used to be Office of Research Risks -- Prevention of Research Risks, Office of Human Research, or whatever it's called now.

SPEAKER: Human -----

DR. WHITE: Yeah. You know, if you go and just present that I would always do that and just get their take on it. If the data is going to be for us, the Best Case Series, we don't do IRB approvals to get that data. And we've actually asked our boards about that and they've told us that this approach doesn't fall into that but prospectively I would recommend it. Yes.

SPEAKER: Two questions. One is why weren't you emphasizing the mainstream ----- and in my opinion of it that those of us who are in the mainstream -- the mainstream -- and had -- I mean, it's kind of sometimes ----- something else. And ----- looking for best case.

DR. WHITE: Right.

SPEAKER: And so my ----- I've never had -----

DR. WHITE: Right, well, that's a good point. The answer to that, though, just to tell you that we do do that to some degree, and I appreciate what your comments are and I think we certainly will try to do it to a greater degree. We actually have found some journals that were put in for free, and we have it. I just noticed the other day that it's in the Oncology Times Journal, which was placed at gratis for us, so we'll certainly look at doing that.

SPEAKER: That's kind of downgrades ----- so, I think ----- and the second point is the question of IRB. If you ----- from Johns Hopkins and other places, a lot of IRBs have become extremely confident ----- whatsoever. And it might be important to inform for you to inform the IRB that they were looking at ----- if somebody wants to look at video flotations. Look for are very stringent, very important, and so it's very important for you to inform the IRB that you are looking at -- I'm in the IRB at my university, and I find that if there is anything ----- go ahead, and they know people in that IRB have been brought up with traditional medical ----- so when they see something different and they might get into trouble, they ----- so, I think it's important for you to tell the IRB that you're willing to back them up. If you don't tell them that you're willing to back them up -----

DR. WHITE: Right. Yes, a prospective situation is certainly a different thing. I mean, it's basically a clinical trial. For us, when we do prospective work, what we're trying to do -- actually, we're just beginning these kinds of projects. We're not delivering the intervention. We're just observing the results of the intervention. So, it ends up being of the -- and we're still going to try to go through IRB approval for that. The only invasive things that we plan to do in those kinds of situations is to do CAT scans, if you consider it invasive, with an I.V. contrast or whatever. But, yes, I think you have a good point. But once you move into the prospective realm, I think you have to follow a lot of rules and regulations of your --

SPEAKER: And so one thing that we are going to do is we set up a study in some country where I know you want to get this stream of data, and so while I like what you're trying to tell us, I think because -----

DR. WHITE: Sure, yes.

SPEAKER: I was just wondering -- you had said that ----- the end point that you're looking for. I was just wondering if you looked at other end points, you know, like in metastases kinds of progression or in quality-of-life ----- end points.

DR. WHITE: Right, that's a good question, and the reason that I put this slide up was just so we could have this dialog along all the issues rather than specific issues. This is about what things

can we do to help you. What are the reasons that you don't -- or, you know, not you personally, but why do you think that practitioners aren't submitting more cases and how can we make the process better. But to answer your question, the reason the Best Case Series is around response is that it is the one outcome that is less confounded by selection bias. I mean, if you look at a complete remission, all right, it is a complete remission, it stands alone. If you look at survival, a patient that has survival of -- let's say a patient has a survival of two years, and you think the median survival for that disease type is one year, well, that's the median survival. So, there is certainly a small -- there is some group of patients that live two years with standard therapy. If you are picking out cases that have that kind of survival, that's not necessarily all that astounding. That's just statistics. So, that survival is a difficult one in this kind of selected case series. Quality of life is difficult retrospectively, because people don't generally gather sufficient data to verify changes in quality of life. It's more -- so subjective. Patient comes in feeling better and so on, that kind of thing. And time to disease progression is the same thing as survival. It's another thing that's confounded by selection bias. Yes.

SPEAKER: I'm sitting here thinking that part of what's come to me is missed opportunity. Missed opportunity. Here we are on the front of, you know, the way we're thinking about medicine. We're thinking about the right to practice this ----- and yet a lot of what I'm hearing is that we haven't approached it. Rather than a fresh new approach, I'm hearing we have to do -- for example, so much is being left out. When you bring back one getting better ----- cases, well, I think part of that is because of the way you formulate what you want to look at. It's a question -- and I think it was Dr. Rosenthal that asked this morning, said what was -- I mean, this is the goal. What works -- you ----- what works? We have to ask a certain type of question that lets you look at the evidence ----- example ----- for me the possibilities. A patient has cancer, it's verifiable, tumor is measurable ----- on medicine. Go through standard chemo, radiation, have a final diagnosis. The evidence is all there. Then the patient chooses, that some weeks later, maybe months later when persistent ----- returns, visible to the patient, recognizable to the patient, but the patient this time chooses not to go back into medical treatment but chooses an alternative ----- and the evidence then that proceeds from that has nothing to do with the medical diagnosis. That to me -- you want to know about that. We want to know about it. We want to have a radio screen as opposed to how do we repackage what we're getting to continue ----- medicine. I'm not saying to eliminate medicine. I'm saying it's to ----- -- and repackaging our approaches to maintain standard medical practices and verifiable evidences, maintaining that --

DR. WHITE: Okay, I got --

SPEAKER: Here's an opportunity. Here's an opportunity, so you keep your secret, thinking it comes from the data. What are you doing or what are you going to do ----- how do you go in an invite the evidence ----- to look at this and accept wholeheartedly what has now returned anecdotal, therefore let's not think about it anymore. But, hey, what works. People out there are having experiences that are working. If you want to have a quality of life -- they are the lucky evidence. How are you looking at that?

DR. WHITE: Okay. I certainly got your point, I think, about that, and you may not like my answer but I'll give you my answer. But, okay, this is the Best Case Series program of the NCI. It

is not the only way to look at complementary and alternative medicine therapies, and I don't at all want you to walk away thinking that I think it is. But what are we trying to do? We're trying to develop enough evidence about an intervention to convince a group of scientifically minded people that this is something that needs to have investment of NCI resources in. That's not a trivial thing to do. And the kind of data that is necessary to make that group convinced is not necessarily -- I mean, there are -- I agree that there are great cases out there that don't meet these criteria, and the reason that we're trying to educate people about what the criteria are is that we don't really want people to come up with cases that might be examples of outcomes that are really important outcomes but they're just not convincing to this group. So, what else -- I would encourage the people that have interventions that don't have the kind of data that we're talking about to try to either think about getting prospective data, or if they don't have the capacity to do that they need to develop either internal networks with other people that are using these kinds of approaches that perhaps can between the network develop that kind of data, or if they can't do that, then try to align with some conventional research. That's one of the big values of this conference -- networking. If you, as a practitioner, have an intervention that you believe works, and you can network with clinical researchers that are willing to take a look at that, if that researcher is willing to go on the basis of the evidence that you've got, then go with it. You know, don't worry about going to the Best Case Series program. I mean, we're just talking about how to get the NCI on board about certain things. And so, if you need some dollars to do that, then come to our funding session and, you know, hopefully we can tell you how you can small pilot projects funded that will gather some data. So, that's the reason -- we are kind of restrictive, but those are the reasons that we are.

SPEAKER: Could you maybe set up a website of practitioners or researchers so we can ----- because I'm out in the middle of nowhere, you know. I'm all by myself. I have no idea where anything is.

DR. WHITE: Right, right, right, right. Yeah, we have actually looked at trying to do something like that, and if we can find the right group of people -- and what I don't want to do is put a lot of time into -- what I want to find is serious practitioners and serious clinical researchers that you can pull together so that there is a real dialog. And there are ways of doing it in a shotgun kind of general approach, and there's a way to do it in a more specific approach in which you're really going to get something out of it. Yes, we have thought about that, and if there are groups that are interested in working with us to do something like that, we would take a harder look at it.

SPEAKER: I had a ----- therapy either in a ----- clinic in Mexico or a clone, and we had a tremendous number of anecdotal ----- questions. One is are we ----- kind of case studies that you're looking for, best case studies. Is there funding to help us administer ----- for people from Mexico. The other is ----- multiple variables that the people doing this every few years have once they go home and ----- kind of process. How will they help us further our mission, which is ----- patient about this particular therapy?

DR. WHITE: Well, it's -- yes, it's minimal to the Gerson therapy as a diet approach with various other components to it, yes. That therapy in and of itself is something that could be looked at. Funding was your second question? When you say "administer," you mean what?

SPEAKER: Gather the information, getting the hospital to set up staff to help us do what you need.

DR. WHITE: All right, so you're talking about prospectively gathering data.

SPEAKER: Right -----

DR. WHITE: Okay, all right, so that's a little different from what we're talking about, but, yes, again -- so, if you want to do a clinical trial of the Gerson therapy, then I think your best bet, being not a research institution, is aligning with one that has an interest in that approach. I mean, if you were at the Gerson Research Institute and wanted to put in a grant application, you certainly could do it probably if you meet the NIH criteria. But I wouldn't recommend it as a solo institution. I would recommend that you align with a cancer research institute, and there are those that have interest in looking at --

SPEAKER: Can you identify those for me?

DR. WHITE: Help you identify some? Yes, let's get together afterward and I can maybe talk to you about groups that have an interest. There might even be people at this conference that have an interest in doing that kind of thing. Your last two questions -- the third one I've forgotten what it was now.

SPEAKER: ----- but people go home, they do it for a number of months, number of years. We don't know what they're doing ----- can you help us design something that, again, helps you ---  
-----

DR. WHITE: Yes, so, again, it's a clinical trial. You have to just design it so that you gather the perspective data in the proper way. You have patients coming back and you develop the questionnaires to get that kind of information. So, that's doable. And what was your last question?

SPEAKER: How will it help us?

DR. WHITE: How's it going to help you? You know, it depends on really what you're interested in. I don't know, really, how to answer it for you as a corporation or whatever, but what I look at the Best Case Series as helping is the whole world. I mean -- I'm sorry, I'm just kind of optimistic that way. So, for the return on the investment that you put into it, I think it is -- if you believe in your therapy, you gather data that will be made available to the larger scientific community and that eventually people will start adopting this and looking at it more seriously.

DR. WU: At the NCI and ----- programming ----- given some thought to the quality assurance issues surrounding eight given alternative therapies, and if so what are some of the steps that are taken to ensure that these kinds of quality and measurement are maintained throughout the study from the inception all the way to when it becomes an awesome few?

DR. WHITE: Right. In Best Case Series, we don't deal with quality issues at all because there's not really a way to do it in a retrospective process. So, if we were to -- let's say someone gives us a Best Case Series on an herbal product and that looks interesting ----- or whatever it is -- and then the next -- the question is what are you going to do with that? Are you going to put it into a clinical trial? Well, that's -- what you just raised is one of the biggest issues about whether or not you should put it into a clinical trial -- is there some quality control for it. So, if after it goes to CAPCAM, CAPCAM says this is interesting information that warrants further investigation and a clinical trial, then will it get into a clinical trial? If it's a nonstandardized approach that you can't do any control on, it might not. You're right. If you do have a pretty consistent way to produce it -- For example, I think PC SPES is probably produced in a fairly consistent way and it's in clinical trials right now -- then, yes, you can get it there. DR. WU: Looking as a person who is inside a ----- outside of NIH ----- how do we go about making sure that ----- there are people that are aware of this -- and I'm thinking of New York -- who just don't want to talk about what they're doing, and they're doing fantastic work. DR. WHITE: Right. I'm glad that issue's come out. The input that we can get back from you on this is helpful. I can tell you that -- you mentioned two people that did come through out Best Case Series program -- Nick Gonzalez and Dr. Burzynski. They happen to be -- Dr. Gonzalez -- well, let's talk about Dr. Burzynski, I guess, has had probably the most problems of many people interacting with the federal government on different levels. But none of that had anything to do, from my point of view, with his involvement in the Best Case Series program. We have zero interest in trying to bring regulatory oversight onto your practice. That is not at all what we are trying to do, and there are no examples that I am aware of, of it being unintended outcome or -- it's certainly not intended outcome of participation in our program. I know that doesn't fully allay people's fears of talking to the government about what they're doing, and I'm willing to consider, you know, other approaches, or some approaches to what can be done. That's an issue that we'd have to dialog about, but I'll just tell you that really -- I think, to me, if you're seriously trying to take a look at your approach, that ought to be somewhat persuasive to people in a regulatory situation, that at least you're trying to gather some data versus if you're trying to do it in some kind of covert manner and not trying to document that there is any value to it, I think you're in a weaker position, so I think there's an advantage to being in the Best Case Series program. DR. WU: No, but does -- I'm thinking about this one group that's doing wonderful work using natural approaches and they don't want to get involved. They don't want so-called media frenzy of Best Case Series ----- and they're really kind of afraid of that big frenzy about, about --

DR. WHITE: Okay, well, that's a good point. I mean, we haven't -- and that's -- well, we have no experience with media frenzy. No, that's actually not true. We have had some small experience in -- Well, I meant out of a result of a Best Case Series presentation. But if what you're saying is should we make some consideration for doing this in a less open kind of -- everything doesn't have to -- Yes. I mean, everything doesn't have to go to the CAPCAM. CAPCAM is the only public forum that sees Best Case Series information. If someone is an advocate for talking to us in some kind of a restricted way about what they're doing because they believe in it and they don't want it to go public, then, yes, we will talk to you. Now, okay, does that mean that it will never get into the public? Well, we're the government, and records can certainly be obtained through Freedom of Information Act requests and things like that, so I can't -- I don't know that there's a way that I can a hundred percent protect people from those. But I'm -- DR. WU: They're medical professionals, they're medical professionals, so they're not really private -- they're not

living in a cave but, you know, they're out in the open and there are things that are scrutinized there in terms of panels, and so ----- and yet, you know, a couple of people have said that they would not -- I tried bringing them here, as a matter of fact, for this meeting ----- they don't want media frenzy and they just want to keep saving lives. And these two cases keep coming up ----- Kelly.

DR. WHITE: Right, right, right. You know, I guess I don't know how to answer it any differently. I mean, there are groups that don't feel that way that have come forward, and we're thankful for them, and I can understand if people feel that somehow they don't -- they'd rather stay in a practice setting and just focus on what they're doing and they're comfortable in that environment, they're concerned about getting outside of that kind of --

DR. WU: ----- further looked at.

DR. WHITE: If talking to us would in some kind of just, you know, informal way would be helpful, we'd be willing to do it. DR. WU: Well, can I take a message back that they can talk to you?

DR. WHITE: Oh, yes, most definitely.

DR. WU: And without a frenzy.

DR. WHITE: Oh, most definitely, yes.

SPEAKER: I was going to leave you a ----- so I wrote it down. I'm not a professional. I'm an 18-year survivor of cancer, and I'm out of my realm, but I'll read you my question. My question is can you use best cases that only use alternative therapies ----- stave off cancer. It seems to me that the only way you can observe the efficacy of all kinds of therapies is to isolate them with no prior conventional therapy ----- results.

DR. WHITE: Yes, those are the ideal cases in the Best Case Series program. I mean, we certainly -- we're not advocating that people receive unconventional approaches for diseases that are curative under conventional therapy. But it would be foolish to think that doesn't happen or that -- or, more or less, not people that are not treatable or curable under conventional therapy, perhaps then what has only taken an alternative intervention. And there is clear documentation for that. That's the optional case that it is not confounded by these other issues.

SPEAKER: Also ----- so what works for one person may not work for others, or it may take longer for therapy to work.

DR. WHITE: Right, yes, yes.

SPEAKER: It's really hard for ----- because you have to -----

DR. WHITE: Yes, so -- I mean, those -- we're really just interested in responses. How many on the panel are? SPEAKER: Ask how many here are survivors.

DR. WHITE: Oh, how many are cancer survivors in the room? Okay.

SPEAKER: And how many both --

DR. WHITE: In both, in both. You're in both categories, all right. Well, you're right, bias is not necessarily an on or off switch. Most people -- Right, no, so what we can say is that we consider it to be a balanced panel with balanced perspectives. What the CAPCAM does is it looks -- it's a committee. It's not -- individuals don't function in seeing data that other individuals don't see. So, it's always a committee decision, so there's a dynamic there, and there is a variety of different people on the CAPCAM, and some of the -- but everyone has some exposure to complimentary and alternative medicine of some sort. But there are people from the FDA on it; there are other government NCI people on it. There are people in the CAM practice community, as she said, so people have different perspectives. But fortunately what we're asking the CAPCAM to do predominantly is to make decisions about whether or not there's sufficient data. I mean, we're asking them to do a relatively circumscribed thing. Does this data -- is it complete? And we generally don't present things that the CAPCAM does not complete, so their answer should be yes. But just where -- to get to there, get there. And if it's complete, does it warrant further investigation. Now, there could be discussion about that. People could say, well, you know, I think this is an interesting approach but we don't know how well standardized it is. Or there could be all kinds of different things that go on in discussion about what next steps are valuable. But I think -- I would -- you know, so, it is my -- I'm just giving you my opinion about the balance of this committee, that in general they've looked at this kind of information, and come back with, I think, reasonable recommendations about what to do. Yes --

SPEAKER: I have maybe one case that I could present to you, but I'm also doing research in identifying markers for cancer with new technology. Is there any avenue that I could submit that?

DR. WHITE: Right. Diagnostic approaches or of something that we usually follow is not what we designed this system for, but -- and it's really much, much better -- can you use retrospective data for that? Yes, sure, you know, but it we'd have to talk about your specific situation. It wouldn't fit into the Best Case Series program but we could talk about how that data might be valuable and then make some determinations about whether or not it warrants prospective evaluation. How much we can help you with it versus perhaps you getting another cancer research group interested in it really depends on -- if you don't have any connections to the research community right now, then perhaps we can direct you a little bit that way, but we might not be the most efficient way for you to get a study going. And the most efficient way is really, I think, to meet a lot of cancer researchers and find the ones that are interested in what you're doing.

SPEAKER: Would you give a little bit about follow-up on the best cases or a little bit -----

DR. WHITE: The ----- oh, no, the advantages, right.

SPEAKER: And -----

DR. WHITE: They were here at the meeting last year -- two homeopathic physicians from India who presented a Best Case Series, and the recommendation was to do a prospective outcomes monitoring and it has been one of the most challenging things, I guess, that I've had to do in this job to try to develop a logistical system to do this and a contract capacity to do it, and actually to do it in a way that those practitioners are comfortable with, to actually have researchers in their clinical environment has so far -- there have been so many issues that have come up just the dynamics of doing this prospective monitoring process that it's really an ongoing negotiation. I wish I could tell you that we were further along. I do anticipate that we're going to get to the completion of a project or the instigation of a project with them, but what it has taught me is that this is not a straightforward -- I mean, we can put it on the slide as a step-wise process, but, you know, we'll get you from step A to step B. It can be a lot of work and a lot of dialog and a lot of understanding other people's positions, and I think we're still in the negotiation phase about that I have to say. If it was an intervention that was better characterized, it probably would have -- because we're having this kind of complexity, it would be better just to put it into a clinical trial, I'd have to say -- to try to get a clinical research group interested in doing a trial, but it is not a well enough characterized approach to have a protocol that you could just turn over to, you know, Institute A -- here's the protocol, implement this protocol and give us back the results. So, that's one of the complexities of it. They practice homeopathy. And it is what they would call -- I guess what should be -- what is frequently called nonclassical homeopathy in that it is a disease-specific intervention versus a patient-specific intervention, so that for lung cancer they have a uniform homeopathic basic intervention. Now, the reason I say it's not well enough characterized is that if you have lung cancer and you have other ailments on top of that, let's say, and you have chest pain or you have something else, then you get the basic lung cancer intervention but you get something else on top of that. And that is just up to their own clinical kind of assessment. So, if we wanted to treat a hundred lung cancer patients according to their system, they wouldn't all get the same thing. So, understanding exactly how to use their clinical approach in a control setting is the complexity. But they use standard homeopathic preparations, mostly that are available different places.

SPEAKER: ----- something else for your chest pain, so I don't think that would be any different. If ----- what they're using, and they're using that for the cancer, that would still be consistent with chemotherapy because we used chemotherapy for stage-end cancer, and then if you get other ailments you get also treated for your other ailments.

DR. WHITE: Yes, but the difference is that in chemotherapy you can demonstrate in the control setting that it's that one chemotherapeutic agent that is having the effect. What we're doing here is looking at somebody's clinical practice. We have a block box in which we have a patient come into the system, receive -- we have 10,000 patients come into the system, receive 10,000 different interventions. Out of the other side we have some patients having responses. But even though the practitioner believes that there's one active therapy that is responsible for all these responses, that's not clear because it's not been a systemized therapy that allows that clinical impression to be verified. I may not be clear about this, but I think the problem is that in a laboratory you can give cytosin or cisplatin to an animal that has a tumor and you see it shrink. In this setting we're not really in that environment, so what we're looking at is a clinical practice versus a specific drug.

SPEAKER: ----- she what she was talking about, this thinking outside of the box, and ----- immune response, then we give radiation, then we do ----- that that itself is a burden load reduction that the ----- then we do ----- of chemotherapy. All that is exactly the same as would happen in the ----- bio-clinical model ----- and something else and something else. And I personally am thinking outside the box now, and ----- don't see any difference in my orthodox training and this way of looking at patients. And I think that her point is very well taken that your CAPCAM people may need to be changed. Maybe you need people like her on CAPCAM rather than somebody with an MD, Ph.D. from, you know, Harvard or NYC. DR.

WHITE: We've got two more minutes, so I think I can answer your question completely. No, it's really a dialog that we're going to have to have about it. I don't disagree that regimens are something that can be effective therapy, and I have to keep refocusing what we're talking about is about this specific Best Case Series thing of how to get an intervention in practice into clinical research. And it's really that one dynamic that is constraining a lot of what we're doing, and I don't disagree that there are other ways to look at this, but I think if what you want to do is to get clinical practice into a controlled clinical research setting, you're going to have to jump over some hurdles that you're going to find pretty much everywhere. But these are sort of the NCI hurdles that you're going to have to jump over, and if there are other setting in which you don't have those hurdles, then, hey, that's great. But, you know, I don't disagree with what you're saying. We've really reached our time. If you'd like to come up and talk with us, we'd be glad to. I appreciate your coming, and please fill out the evaluation forms.

\* \* \* \* \*