represent tens of thousands of men who, like me, are concerned that some day their therapies will no longer be effective. We are keenly aware of the need for more drugs and for more effective drugs for late-stage disease. We know that individuals have different responses to drugs and we know that combinations of drugs often are superior to individual drugs. That means there is an urgent need for options.

I would like to also emphasize that we survivors do not expect a perfect world. While the media love to highlight adverse news, such as news about unexpected drug side effects and complications of approved drugs, we survivors want access to drugs that have a reasonable balance of benefit to risk. We are willing to take reasonable chances. I like what I have learned about satraplatin. Please recommend approval and give us this new option.

MS. CLIFFORD: Thank you. Our next speaker is Thomas Kirk.

MR. KIEFERT: For those of you who know Tom

Kirk, who Tom Kirk is, I am not. Tom Kirk is the president and CEO of Us TOO International. My name is Jim Kiefert. I am chairman of the board of directors of Us TOO International, a survivor, and we thought it would be better if a survivor was talking about our survival.

My name is Jim Kiefert. I was diagnosed with prostate cancer in 1989 at age 50. I had a PSA of 39 and the only options back then were radiation and surgery so I decided to have surgery, and when the doc came back and said, you know, your PSA is supposed to really go down a lot after your surgery and it didn't, I guess it must have spread beyond the gland so let's try radiation. So, they did radiation of the prostate bed and my PSA still didn't go down after a year. He called me in his office and he said, Jim, I have to tell you, you probably have one to three years to live. You had better go home and get your life in order. It will be 18 years in October that he told me that.

I say this as a lawyer, and I have used everything at my disposal, those FDA approved

treatments and any other treatment from meditation, prayer, herbs, anything that I can to help strengthen my immune system and fight this off. I hold a doctor's degree in education. I spent 41 years as an educator. I retired as a school superintendent. I was a university professor at Washington State University and taught math and science. I live in Olympia, Washington where I serve as chairman of the Washington State Prostate Cancer Coalition Task Force. I also read proposals for the Department of Defense and I am on the SPOR Patient Advocacy Committee and the Department of Defense has asked me to serve on a committee to look at prostate cancer research protocols. I have been chairman of the board of directors for Us TOO International since January of 2005.

Us TOO International does not endorse any products or services, and that is a part of our board policy, and we do not, and will not endorse any product or service. I have not received any compensation for my travel here. Us TOO does receive unrestricted educational grants from a

number of pharmaceuticals, including GPC Biotech. I am here today to tell you a little bit about Us TOO and why we are looking for more options with prostate cancer.

Us TOO was formed in 1990 by a group of survivors and their families, and at that time--like when I was diagnosed in 1998 I didn't even known I had a prostate. I used to call it a prostrate and my wife kept correcting meB-this group of survivors decided to form a group to spread out and we now have 325 chapters throughout the United States and throughout the world. We have a monthly newsletter that goes out, called "The Hot Sheets" and when Tom and I go to the AUA meeting or the ASCO meeting we meet physicians from across the world that are looking at our website and using our "Hot Sheets," translating them into various languages. Our website gets about 360,000 hits a month from men looking for information about prostate cancer.

We also belong to an organization, and that is what our blue ribbons here are about. It

is called Raise a Voice. We found that the prostate cancer community was not pulling together on issues so a number of prostate cancer patient advocacy groups formed a group called Raise a Voice. Our board of directors at Us TOO accepted the policy, and the policy is that we want to have access to treatments for advanced prostate cancer as soon as possible.

We know that in the last 40 years there has only been one drug approved that has had survival benefit for prostate cancer, and that is taxotereB-one in 40 years. That is disgraceful. So, when men start becoming androgen independent, when the hormones no longer work they have one thing to look forward to and that is chemotherapy, which they don't look forward to gleefully, as you might guess.

Anyway, I am here to represent the prostate cancer community. I want you to look around the room here. There is just about the right number of men in the United States here that are going to die today of prostate cancer. About

80 men every day in the United States die of prostate cancer. We need options for these men.

I run a support group in Olympia, Washington and I watch men. I have become friends with them. I know their families. And, they go through their options and they die a very painful, excruciating death. And, we are asking ODAC and FDA to help us approve and make available treatments that will give men some hope. We are concerned about safety. Physicians do no harm, but they become very desperate when there is nothing left for them except the chemotherapy and when that fails it is "get your life in order."

Anyway, I appreciate all your hard work. It is not easy to do this, to evaluate all these treatments, and we appreciate everything you are doing for our prostate cancer community. Thank you. MR. CLIFFORD: Thank you, Mr. Kiefert. Our next speaker is Katherine Meade.

MS. MEADE: Hello. My name is Kathy Meade. I am active with several cancer-related groups. The SPOR advocates, patient advocates and research

and the Virginia Cancer Action Plan which are general cancer groups. I am on the board of the Virginia Prostate Cancer Coalition and the national alliance of state prostate cancer coalitions.

I am here today representing all cancer patients, especially prostate cancer men on behalf of Raise a Voice. I have no connection with the company producing the medication that is being discussed today.

It is important to remember why we are all here, the advocates, the FDA, the pharmaceutical companies and the review committee, we are all here on behalf of the welfare of men dealing with prostate cancer and you have heard some of them speaking today.

In reviewing the materials for today's presentation, I found a quote from an ovarian cancer patient that exemplifies the struggle of all cancer patients dealing with end-stages of a terminal disease and the difficulties of current treatments. She said, after the first chemo I spent most of the week wondering how I would react.

What would the side effects be like this time? Would they get worse? Will this treatment work? What if it doesn't? So far I am doing okay, but trying to take my focus off of all these questions can be challenging at times. I honestly feel like this should be old hat for me and I should be far more at ease and comfortable with the balance of undergoing treatment and my daily life. But recently, talking to others who are living with cancer, I am reminded that it is okay to be confused, angry and even frightened. It is just not okay to let go of the control of the rest of your life.

We need you to help the men with prostate cancer find ways to not let aggressive prostate cancer control the rest of their lives. There are two men who I know would be here today to talk to you but, unfortunately, they are lost to us. Tom Witte and Mike Rice were both tireless advocates for men with prostate cancer, doing whatever they could to lead the way to new effective treatments that allow men to lead a good life with the time

they have left. They both actively participated in clinical trials that they were eligible for. They also both gave the ultimate gift at the end of their lives. They donated their bodies for medical research, Mike to the warm autopsy program at the University of Michigan; Tom to a scientific program in Philadelphia.

You were supposed to be handed little pieces, which I have produced, on these two men. It is hot in here; we are crowded. I am sure everybody wants to go home. I would appreciate it if you would read this just a little bit to know who they are, and I don't need to go into a lot of detail about them.

I got involved in cancer advocacy when my husband Bill was diagnosed with prostate cancer. Two hears after his diagnosis he was diagnosed with a second primary cancer in his lungs. At that time he was treated with taxol and carboplatin. The treatment was difficult but he did what he had to do to stay alive for me as long as possible. The oncologist told me that he felt the major cause of

his side effects was the carboplatin. I am hoping with this new formulation of a platin-based treatment and also with an oral administration some of the side effects that Bill experienced will lessen significantly. I lost Bill in 1998.

We want and need more options for men at end-stage disease or to keep them from reaching end stage. Our first choice would be treatments with minimal side effects but, unfortunately, that is not the case with most chemotherapies. But if they extend lives it will be worth the extra time for at least some of the men, if not all of the men. Unfortunately, because of the side effects, some men will bypass chemotherapy.

We are here today, at the end point of the donations of the men who participated in the clinical trials to review this new treatment for prostate cancer. If it is safe and if it extends the lives of men dealing with this devastating disease, I urge you to approve satraplatin and remember both Mike and Tom when you go through the process. Thank you.

MS. CLIFFORD: Thank you. Our final speaker is Dr. Nissenberg.

MS. NISSENBERG: Good afternoon. I am Merel Nissenberg. I am an attorney in private practice in San Diego, California but, more importantly, I am president of the California Prostate Cancer Coalition and the National Alliance of State Prostate Cancer Coalitions. So, while I am not a prostate cancer survivor, I am here today to represent thousand and thousands of men, their families and their caregivers. We have 33-plus states already in the National Alliance. We are not three years old. And, that represents statewide of support groups from one end of each state to the other. So, we are talking about a lot of patients.

I have received no financial assistance for attending here today and I have no conflict of interest. I am here simply to talk about hope and meeting an unmet need, and it is for a specific cohort of patients for whom chemotherapy has failed and for whom there are no other standard options.

One of the benefits of satraplatin is its oral administration which has been not talked about too much today, but that is very important and it certainly benefits the quality of life for these men. The disease-free survival or the progression-free survival we have heard today can also be a surrogate for overall survival. Moreover, I would submit that even if survival overall were not benefitted, the pain relief that these men would get from this drug would certainly be worthwhile to them and is something that they should have the option to qualify for.

I also think that the SPARC data, having to do with prior chemotherapy, the fact that taxotere has been more beneficial as shown in prior studies is really in opposite to this discussion. The point is that this drug is clinically relevant for these men, a very special group of men, and we are here today to ask that you recommend its accelerated approval; that you provide hope; that you meet a declared unmet need in future research. Thank you.

DR. ECKHARDT: Thank you. The open public hearing has now been concluded and we will no longer take comments from the audience. However, we are going to go on to a break for about ten minutes before reconvening. And, I need to remind you to refrain from any discussions about this application. Thank you.

[Brief recess]

DR. ECKHARDT: What we are going to start out with is a brief summary from the FDA, again reminding us about the accelerated approval process.

DR. JUSTICE: Since GCP Biotech is seeking Subpart H or accelerated approval for satraplatin, I would like to say a few words about that type of approval, for new members of the committee.

Accelerated approval is an approval based on a demonstrated effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. Accelerated approval requires that the applicant conduct a study to demonstrate clinical benefit. However, clinical benefits such as

improvement in survival can be demonstrated in the same study as proposed by GPC Biotech or in another postmarketing study which will usually be under way at the time of approval.

What accelerated approval is not is an approval based on an uncertain effect on an efficacy endpoint or an effect on an endpoint that is not reasonably likely to predict clinical benefit.

Please consider this during your deliberations. Thank you. Was that clear?

DR. ECKHARDT: Yes, thank you. Any questions about that briefly? Yes?

DR. DAHUT: If one has an accelerated approval and the definitive endpoint is not positive, what are the options for the FDA?

DR. PAZDUR: Well, there are provisions that the drug could be taken off the market, however, obviously that is a very difficult process to do. That is not something that we take lightly. For those of you who have not been on this committee, we have had two ODACs in the experience

of some of the members here where we have gone over accelerated approval commitments. Okay? There are varying successes with these accelerated approval commitments, various timelines that people have had. We have had drugs that have been out there for eight years that have not demonstrated clinical benefit, and one of the reasons that we have brought this to the committee is that we really take this as a very serious type of approval.

We want this discussed with the FDA. We want to be sure that there is some reasonable likeliness here that we are going to see an effect on a clinically meaningful endpoint such as, in this case, overall survival. So, one of the things that I think we have to come in some discussion with, and I hope in your deliberations and comments you will comment on this whole issue of the link between this endpoint, this composite endpoint with all of its components, and a potential link to overall survival.

Remember, we are not asking that this be an established surrogate or a definite surrogate,

but there has to be a reasonable likelihood that the effect that we are seeing on this composite endpoint would translate into overall survival.

Questions from the Committee

DR. ECKHARD: Thank you. What we would like to do next is to move on to questions to the sponsor or to the FDA. We are going to need to, hopefully, focus on ones that are the most burning since we, hopefully, need to get to the FDA questions to us specifically.

I would actually like to start out with a question to the sponsor. We have seen quite a bit of data with regards to adjudication for a radiology standpoint, and it seems as if there was an external review committee that went over sort of the medical oncology aspects of progression. What I didn't see was how that went, you know, what percentage, what types of discrepancies there were between the medical progressions versus the radiological progressions, and which way those went when they were adjudicated.

DR. ROZENCWEIG: I would like to ask to the

podium Dr. Siegelman to discuss part of this aspect. Dr. Siegelman is head of the MRI department at Penn and he has extensive experience involving blinding radiologic assessment. And, I will complete the answer.

DR. ECKHARDT: I was actually talking about the non-radiological adjudication because you did have an IRC that actually was a medical oncology review of the non-radiological progressors.

DR. ROZENCWEIG: Right. The way it worked, there were really two parts in this review. There were first two radiology readers who reviewed all the x-rays and scans totally independently. They even didn't know who the other reader was. And, they decided upon progression, no progression or if there was a progression-free, as was explained earlier.

After that, there was a review by two clinical oncologists and these two clinical oncologists worked together and reviewed clinical details one by one. They reviewed, for example, first all the PPI scores, all the PSA, all the

performance status, etc. Then, when everything was adjudicated they had also access to the opinion of the radiologists and they then decided, based on all the information that they had, if the first event that would be counted in the PFS would be the radiology event or one of the other events like PPI increase or analgesic increase, etc.

DR. ECKHARDT: Just briefly, did you have a sense of how many of the ones that were not based upon radiological changes were adjudicated or changed somehow during that review?

DR. ROZENCWEIG: These are not adjudicated because they worked together and so they had to reach a consensus. The two radiologists worked independently. They had no idea how the other radiologist would assess the case.

DR. ECKHARDT: Dr. Mortimer?

DR. MORTIMER: I have a question regarding intravenous bisphosphonate, so IV bisphosphonates for an indication of a skeletal-related event, but there were 30 percent of individuals who were also taking bisphosphonates and I wondered what impact

that had on outcomes.

DR. ROZENCWEIG: We have actually data showing the pain effect. I can show you this.

DR. MORTIMER: My concern is obviously was there a disproportionate number getting IV bisphosphonates that offset pain or disease progression?

DR. ROZENCWEIG: I can show you first bisphosphonate or no bisphosphonate had no effect on the primary endpoint.

[Slide]

I am told that this line is not visible here. That is the unit. Here you have the bisphosphonate and the no bisphosphonate groups. We have looked at responses, especially responses with satraplatin and, in fact, the response rate in patients with higher bisphosphonate is actually highly significant. The difference between satraplatin and placebo is actually very significant in patients who were receiving bisphosphonate.

DR. MORTIMER: I am sorry, I don't mean to

be thick but in favor of what? Mor patients responded to satraplatin if they had gotten bisphosphonates?

DR. ROZENCWEIG: No, no, among the patients who received bisphosphonate the difference in pain response favored satraplatin and the difference was highly significant.

DR. ECKHARDT: Dr. Perry?

DR. PERRY: [Off microphone].

DR. ECKHARDT: Dr. Wilson was next.

DR. WILSON: I would like to get some of your thoughts on the pain endpoint. We can see from the Kaplan-Meier curves that the median radiographic progression for both groups was around 10 to 11 months. Yet, when we look at the median time to pain it was around 25 months for the control group and 70 months for the treatment group. So, it appears from this as though the benefit of this drug was lasting even after the patients had radiographic progression and, presumably, went off the drug. This rates as a question to me not so much as to whether or not the

benefit was that long-lasting but whether or not there really was a problem with this endpoint.

The second part of my question is to turn to your analysis--

DR. FARRAR: I am sorry, which slide are you looking at?

DR. WILSON: I am looking at the briefing book here. The next part is when you looked at the relationship of the response of pain and survival you, in fact, showed on page 21 that there was a very marked benefit in the survival for those patients that had a response in terms of pain. But in your study you weren't looking at responsive pain but you are looking at time to pain worsening or increased opioid use. The benefit that you saw in terms of response to pain, translating into a survival benefit which is quite marked, certainly is not seen when you look at the overall survival benefit in both arms. The curves are pretty much superimposed.

So, both of these questions, to me, really raise the questions that have already been raised

as to whether or not the pain endpoint really reflects the degree of clinical benefit that might seem to be on the surface because, for me, in the absence of a survival benefit that is the only clinical benefit you have really shown for this drug at the present time.

[Slide]

DR. ROZENCWEIG: Let me show you again the landmark analysis at three months. I realize that the pain response was not the primary and not the secondary endpoint, however, it was a prespecified endpoint and we looked particularly at the metrics to justify the use of the analgesic score, the PPI score that was used to determine the response rate. So, in that sense it has some validity.

I realize that when you do a responder versus a non-responder analysis you always have a potential bias. However, what is interesting here is that this was done at three months, so at 13 weeks, and 80 percent of the patients had already achieved the response by week eight. Even if you take the 20 percent of the late responders and you

add them to the non-responder group in this landmark analysis the difference still remains very significant in favor of satraplatin.

So, we think that this landmark analysis is really extraordinarily strong and actually I have never seen in prostate cancer such a relationship between a pain outcome and survival, and I think this is really solid and the data are there to show it.

Now, how it relates to survival in general it is difficult to say. We have only 25 percent of the patients who do have a response rate if you take the entire population. However, if you look at one of the slides that I presented showing the effect over the entire duration of the study, if you look at the 50 percent reduction in PPI over time from the beginning to the end of the study, week after week, we have it here for non-NSAIDs but it is seen for all the patients. You can see that, in fact, this benefit is there during the entire observation period.

One of the complications in understanding

the relationship between these endpoints is related to the IRC process because what is important here of the primary endpoint is the PFS based on IRC assessment. That was not necessarily the PFS based on the investigator assessment. So, sometimes, you know, if the IRC decided that progression occurred earlier you have follow-up information. If they didn't decide that it may have worked the other way around. So, that is a little bit complicated, you know, to really put these metrics together because of that aspect.

DR. ECKHARDT: Dr. Farrar, did you want to make a comment?

DR. FARRAR: Yes, and there are a couple of things to comment on but let me start with that graph, if we could go back to that graph for a minute. There is a problem with the graph. Let me back up and say that I think that you have a study that demonstrates some benefit in pain to this group of patients. This graph, however, is predicting the probability-Bgo back to the landmarkB-which is that basically what it says is

that if you have less pain you are more likely to survive a longer time. And, I am completely willing to accept that. That makes great sense to me. Obviously, the amount of pain you have is not a bad surrogate marker for the amount of disease you have.

What it does not say is that treating that pain with this drug improves survival. You can't make that leap. I don't know that if I treated this patient with opioids or did a good job of NSAIDs or bisphosphonates or other treatments whether I would have gotten the same effect. So, I don't dispute this. I just have trouble accepting this as supportive for the particular drug in question.

DR. ROZENCWEIG: Sorry, so you are saying that this graph supports the efficacy of satraplatin. We have never claimed that this was meant to be better than any other treatment. This is just response to satraplatin and we showed that the responders live longer than those who don't.

DR. FARRAR: Okay. I think the issue here

is that the people who have respondedB-here it is responders and non-responders. Is this only in the treated group? Where is your placebo group here?

DR. ROZENCWEIG: No, this is just all patients.

DR. FARRAR: I agree, and that is exactly the right analysis but it doesn't show the difference between your drug and the placebo group. You know, I am not downplaying the interestingB-I mean, I find this very interesting. I would love to look at the data later with some other issues, but the point is it doesn't support your drug over placebo.

Similarly, a number of the other nice graphs that you showed us were done on evaluable patients. Right? So, the people who survived that period of time were included in those graphs. In general, in the design of pain studiesB-I don't know about oncology studies but in pain studies the issue is you need to take into consideration even thoseB-or consider the data of people and what it might have been if they had survived. There is an

argument about whether you do baseline observation or last observation carried forward, but my brief analysis of the number of people who weren't in the study suggests that those graphs would be a lot closer together if you, in fact, did either baseline or last observation carried forward.

So, I don't argue with you and I think that your data does show that there is a difference in pain. Where I come down is does that mean that there is a benefit in terms of survival? You have not done the final analysis there. You have presented some data that suggest that there is a trend. I am fully willing to believe that when you get to the full number you probably will be able to show it being statistically significant, and I leave it to the committee to decide whether that is true or not. But we need to know that because, you know, we don't know whether long-term treatment with this leads to something else, kidney failure or other things that would lessen the amount of survival.

So, the real issue for me, if you could go

to slide number 45.

[Slide]

Here what you suggested was that if you took out the pain progression that there remained a benefit in terms of progression-free survival. I had trouble looking at that in conjunction with slide 14, presented by Dr. Cohen and in other data that is presented, where it looked like the predominant feature that predicted the benefit was the pain finding. In fact, if you look at the PFS events in slide 14B-I don't know if you can show slide 14, Dr. Cohen.

[Slide]

Here what it says is that the PFS events were less for your product in terms of pain, 43 percent on prednisone and 35, and slightly less, one percent, with radiologic findings. But the others, the deaths, the PFS weight and the other causes for progression-free survival dropout were higher. So, I have trouble knowing how that in your slide, which showed that when you excluded the pain events you still got significance. Because

where I come down with all this is that my issue is-Band, as I said, I am happy to believe that when you get to the final numbers you will show some benefit, or I hope you do. I mean, I take very seriously the issues that are brought up by our speakers from the floor and I wish very strongly that we had a good drug to treat this disease. But as a pain specialist and somebody who sees these patients in clinic, I know that most of our patients are inadequately treated with analgesics. They don't get enough nonsteroidals. This is a very responsive disease in terms of the pain for nonsteroidals. Bisphosphonate works. There are other things that work. I worry about putting them at risk for side effects, long tem, short term. I worry about in trying to get you to see your son graduate from law school that you might die from a nadir effect of the low white count earlier, or that you might miss some major event because you are throwing up secondary to chemotherapy. And, I think it is really that issue that I am trying to struggle with and that I am having trouble with.

I don't know how to interpret this slide 45, and if you could help me, that would be helpful.

DR. ROZENCWEIG: Could I have one of the slides that I presented with the type of progressions, the equivalent of the slide that was just shown?

[Slide]

So, what you have here is the distribution of first PFS events. For example, we have more deaths in this group, as you noted, but these are not deaths on study. The deaths on study are actually more frequent on placebo and these are patients who had no progression according to the IRC and no information until death as a PFS event. So, that is not an adverse observation. It is just a question of stratification.

If you look at the skeletal events, you also note here an imbalance with a suggestion of a higher proportion of skeletal events. This, again, is the proportion of skeletal events as first PFS event per the IRC. In reality, if you look at all

the skeletal events in the study we have 11 to 12 percent of skeletal events in the study and it is exactly the same in both arms. So, this table has to be interpreted with some caution.

DR. FARRAR: Do you have a slide with those other data on it?

DR. ROZENCWEIG: I have a slide on the skeletal events.

[Slide]

This is, for example, for the skeletal-related events and, as you can see, the total of skeletal-related events, if you take all of them, it is 12 percent in the satraplatin arm and 11 percent in the placebo arm. But if you look at the skeletal-related events as first events it looks like you have more in the satraplatin arm than in the placebo arm, but it is not really reflective of what happened in the study. It is reflective of what was considered as first event for PFS events.

DR. FARRAR: So, the slide that you showed us is if you remove the pain-related event and went

on to subsequent non-pain-related event you are still able to show some benefit for the drug.

DR. ROZENCWEIG: Right.

DR. ECKHARDT: Let's move on. Dr. Harrington?

DR. HARRINGTON: Thanks. One question about timing here, and this is a question related to the accelerated approval. So, we have heard two different estimates of when the survival data will be available. The FDA indicated that they were told by the end of 2007; the sponsor says a little bit later. So, first, can I get some clarity from the sponsor about when the survival data will be available, the full survival data? Second, then, from the FDA, how that fits in the timing of how long it takes an agent to get on the market from accelerated approval. In other words, are we talking about a meaningful difference here if we are waiting a few months for the additional survival data, and it is going to take at least that long after a hearing such as this for the accelerated approval to be official?

DR. ROZENCWEIG: First, let me say that the notion that the analysis would be available by the end of the year is based on a statement that we made to the FDA. But we made that statement to the FDA based on an estimate of several weeks ago, actually back in May, based on event rate at the time. What we have seen recently is that it seems like the event rate is slowing down tremendously. We are down at five events per month or less. If that trend continues, and that is new and it is very different from the kind of event rate that we had when we met with the agency at the time of the filingB-if that trend continues it is going to take much longer to reach the 700 events.

DR. HARRINGTON: How much longer?

DR. ROZENCWEIG: Well, I think it may take probably another year until we have these events because if they go down continuously, you know, we need to have the events; we need to analyze the events; it has to be prepared. That could take about one year or more.

DR. HARRINGTON: So, Dr. Pazdur, if this

drug were to gain accelerated approval, what benefit would that be--

DR. PAZDUR: Well, accelerated and full approval as far as a timeline goes is really no difference. What happens usually is that after this meeting there are labeling negotiations. Obviously, there are other reviews that have to be considered. We are talking about the clinical review; are there outstanding manufacturing issues; clinical pharmacology issues; pharm tox issues that all have to be brought into this. But in general we are talking about a few months here.

One of the things I want to emphasize though is that this time difference should not be the ultimate opinion maker here. Other access to unavailable drugs or unapproved drugs does exist, such as expanded access programs, treatment INDs, etc. that even allow charging for drugs and I think people have to be aware of this, that those are also some of the other alternatives to get unapproved drugs to patients that need these drugs.

DR. ROZENCWEIG: If I may though, expanded

access is not easy access and, you know, this doesn't really make the drug available easily to other patients. It is a very complicated, cumbersome process and the fact that we could charge for it is not really the issue.

DR. PAZDUR: We do agree that the best access is obviously drug approval, but there are alternative mechanisms that are available. Some drugs that have had expanded access have treated 20,000 patients, 15,000 patients, 10,000 patients. So, you know, it is a method that some companies have used to get access of drugs to patients while there is either review of an NDA or completion of pivotal trials.

DR. HARRINGTON: Thank you. One more question which may have been answered in your responses to Dr. Farrar, but I am not sure because I am not sure I understood all those responses. So, could we have your slide 15, please, that shows progression-free survival, or 13 is actually the one I want, progression-free survival IRC adjudicated?

[Slide]

There it is. So, one of the things that a statistician notices here and, of course, everybody notices right away is that these are not proportional hazards. But beyond the technical point there, these curves separated at about ten weeks. Before that, the effect of the placebo plus prednisone and the satraplatin plus prednisone appear to be equal.

So, I would like you to help me a little bit understand what is happening prior to ten weeks and post ten weeks. Are you seeing one type of progression prior to ten weeks and then something very different post ten weeks? I think where my question is headed is if that separation in those curves is largely due to pain progressions, that is where I think some of the problems that some of us have with the use of the instrument come into play. So, do you know the natures of those progressions before and after ten weeks?

DR. ROZENCWEIG: Well, obviously, before ten weeks we didn't have radiographic progressions

because the first scheduled time for radiographic progression was at ten weeks. So, where the proportion of radiographic progressions starts to increase is at nine weeks and ten weeks. So, definitely most of the progressions that you see before ten weeks are related to pain.

But let me correct one statement which I think I heard, and that is the variance hazard ratio in the curves.

[Slide]

If I may show the slide, here are the hazard ratios over the entire curve and they are fairly parallel, and certainly the assumption for the model I think was met.

DR. HARRINGTON: Yes, I am less worried about the assumptions for the model than trying to get an understanding of the nature of the progressions. So, thank you for the explanation about when the radiographic progressions were occurring versus the other ones.

DR. ECKHARDT: Dr. Grillo-Lopez, I know you are leaving. So?

DR. GRILLO-LOPEZ: I have a question for the sponsor, and the background is as follows, the agency believes strongly that overall survival is a very important endpoint. Therefore, I can easily understand that an accelerated approval, particularly when an overall endpoint is spanning a year, or whatever time, puts them at a certain risk because that endpoint might not happen. It might not support the accelerated approval. However, what this committee has to do today, your task, is to recommend or not for accelerated approval regardless of the fact that there is a pending part of the study that will yield some information on overall survival.

So, tempting as it might be to say, well, let's defer until we have overall survival information, that is not our task today. That is the FDA question but for accelerated approval your task is to decide whether you recommend it or not based on the data that you have today because otherwise we would not have accelerated approval. It would always be full approval and we would

always be doing overall survival as an endpoint rather than the surrogates. So, I believe that you have to make your decisions and your recommendations disregarding overall survival for now. It will come back to this committee later.

But then I also think that you need to consider whether overall survival at all will be useful, and that is where my question to the sponsor comes in. For patients in either arm of the study is the protocol providing any way of randomizing or balancing or ascertaining what subsequent therapies these patients will get? Because, if it isn't, if your answer is no, then I would say that endpoint is useless because you have no idea whether the patients will get treatment or not; whether it will be chemo or something else. You will have no control over that. You have no way of knowing, even if they do get chemo, even if it is docetaxel, is there any balance between patients on either arm of the study. It is a totally uncontrolled part of the study. So, that is why I ask the question of the sponsor.

DR. ROZENCWEIG: No, there were no provisions in the protocol for subsequent chemotherapy. Remember that at the time the study was initiated the only drug that was approved and used was mitoxantrone. I would like to ask Dr. Petrylak to perhaps comment on this.

DR. PETRYLAK: Yes, as the PI on the SWOG 9916 study, as well as being involved in TAX 327, in those particular studies there was also no provision for what the second-line chemotherapy was. So, neither of those studies had that level of, should I say, rigor in determining what the other studies are. The types of treatments that these patients would receive in the community, none of those particular treatments have also demonstrated survival, whether that be mitoxantrone, whether that be navalbene, whether that be cytoxan. So, the question, of course, is difficult to answer but the precedent from the other studies has not the been set.

DR. ECKHARDT: Miss Haylock, you had a question?

MS. HAYLOCK: There were several questions in regards to the instrument for monitoring or measuring pain so I wonder if the sponsor could address the questions or concerns of the language translation and so-called tweaking of the PPI, and the issue of score averaging? That is one issue.

Then, the second one, could you talk about the international variations of pain management, access and availability of opioids in these various countries? Because I know that in the Eastern Bloc European countries it is difficult to get those drugs. So, I just wondered if you could comment on that, please.

DR. ROZENCWEIG: Yes, I would like to ask Dr. Charles Cleeland to comment on this question. Dr. Cleeland is chair of the department of symptom research at MD Anderson. He is the developer of the BPI pain scale, one of the most widely used pain scales worldwide.

DR. CLEELAND: Thanks very much. I am a later-comer to looking at these data. I was called a couple of weeks ago, given a little description

of the study over the phone and I said, oh, my gracious, the pain measurement is, indeed, a difficult one. Several people have pointed out that if we are not able to justify the pain measure that is very difficult.

So, I began to think about the data and began to ask the sponsor for the kinds of information that would help me make a judgment about what exactly happened.

[Slide]

Here you see the diary for the patient. The patient actually used numbers and you don't see the horrible, and excruciating, and so forth, here. Those were casually translated. I had concern about that. But if, in fact, the patient was using this as a numeric scale it falls within a long tradition of using simple numeric scales and diaries for the assessment of pain. We do know that the simple numeric scales work very well from some of our earlier work with the WHO across different populations. So, that was a little bit of comfort.

[Slide]

I think the next reference point is we had the FDA speak about the new guidelines, and it is critical for all of us that these be PROs be carefully evaluated. However, I think in that document they acknowledge that some scales are pretty robust and we ask our patients clinically 0-10 pain questions every day in the office. They did, in fact, note that a single item is a reliable, valid measure of the concept of interest, e.g., pain severity and, therefore, one-item PRO instrument may be a reasonable measure to support a claim or concepts. So, there we have language that kind of opens the door should this, in fact, be a numeric scale. So, we did take a look at some of the data.

One of the questions I had for them before I even began was let's take a look at survival and this pain response as a way of validation. If you go out five weeks it looks a lot better.

[Slide]

But, in fact, if you do look at baseline

you see that the patients who have substantial pain are those that die earlier. So, there was essentially a connection with a solid endpoint in the pain measure.

[Slide]

So, we talked a little bit in the introduction about some of the psychometric properties and I would like to go over those just briefly again as they were brought up by Dr. Basch. Inter-rater reliability, here the patient is recording just a number so that is not an issue. There was an issue in the coding of the analgesics because these were from many countries and there had to be some consensus on that. Internal consistency on a single item really is something that we can't calculate. It exists in and of itself. So, when you have two or more items you would require that internal consistency.

The other thing I asked them to do for me was to look at the mean and standard deviation of these patients prostate cancer at baseline. Okay? And combine that and give me a sense of the

variance at baseline. It turns out that the standard deviation of that measure at baseline was approximately 1, and there are a lots of ways of approaching clinical significance, and that could be a debate and we are continuing that debate. But it is reasonable to think that I think people would generally agree if you are willing to use distribution-based approaches that half a standard deviation isn't bad. What rides in this study is essentially changes of a full standard deviation in the pain score. So, again, I was a little more pleased with the data that I was looking at.

[Slide]

I was very upset to hear that they used the McGill-Melzack because, working with the WHO and a lot of studies cross-nationally, patients have a real hard time translating and understanding horrible and excruciating. That is why we really push using just simple 0-10 scales that patients have. But we asked another question, and I think this was critical, what was the variance in these pain reports that was generated by ways of breaking

it down that might reflect a bias, a linguistic bias or a cultural bias, and it turns out it didn't account for much.

So, in sum, we have a scale that sure looks like a numeric scale and we all use those numeric scale in pain trials. It behaves like a numeric pain scale. I mean, there are lots of ways of approaching this problem of cultural equivalence but this simple pain scale doesn't seem to vary a great deal dependent upon the country it used and the language it used.

Now, there was a site effect. It is small but I think that is the second part of your question. Yes, there is a substantial difference in pain management across these various sites and that presents an interpretation problem across these various sites. But what you want to look for is effects that perhaps rise above that variance.

DR. ECKHARDT: Thank you. We are sort of running out of time but I have three people on my list that had questions, and that is Drs. Richardson, Brawley and Dahut. So, if you can just

try to get us through these questions briefly. Dr. Richardson?

DR. RICHARDSON: Gail, I hardly know where to begin. I am just curious, having been around a number of years, why the sponsor chose this particular composite endpoint. I mean, there are a number of techniques for trying to assess response to chemotherapy going back to the pre-PSA eras, and I guess I am curious why those kinds of scoring systems weren't used, or at least why there was no attempt to incorporate PSA into kind of response criteria.

I think if you look at the endpoint criteria on slide number 6 by Dr. Rozencweig, these generally take months to develop, whereas some of the biochemical markers that a person might be looking at, rising PSA, alkaline phosphatase, even acid phosphatase levels show progression much more quickly. I suppose the cynic in me leads me to think that the intent is to treat a lot and look but not too closely at some of these patients.

The other question I have is with respect

to objective responses. There is a complete response and a partial response rate of eight percent in patients with soft tissue disease. Were there no bone scan or x-ray responses?

DR. ROZENCWEIG: I would like to ask Dr. Petrylak to comment on the selection of the endpoint, but let me briefly state that we agreed with the agency that PSA could not be used in the PFS endpoint. I might add that we have some sensitivity analyses that I have not shared with you including the PSA, and basically when we do that it doesn't really change anything in the results.

In terms of the responders, I am sure Dr. Petrylak will comment on this, this is a very difficult disease to evaluate. That is the problem with prostate cancer. They have osteoblastic lesions most of the time and you are really left with death, you know, in terms of the evaluation. So, you cannot really compare prostate cancer to other tumor types like, for example, breast cancer where you have lots of pulmonary changes,

superficial lymph nodes, etc.

DR. PETRYLAK: When we designed the SPARC trial we wanted to come up with every possible method of progression that was evaluate in other studies, and we recognized that PSA was not an endpoint that the FDA was going to accept. In fact, in our retrospective data from SWOG 9916 we found that 30 percent decline does correlate with survival, but that data was not available to us at that particular time. So, we basically wanted to be as rigorous as we could to find every way that we could find for failure of this particular drug and look at clinically relevant endpoints, things that somebody would use in practice on an everyday basis.

The second issue, of course, is with bone scans. In my experience and being the PI of SWOG 9916, it was rare that we saw a bone scan response. In fact, these responses were in those patients who had been on drug for a prolonged period of time. So, bone scan responses was something that we really could not use to assess efficacy.

It is interesting that we do have a significant difference in the objective response rate. That is something that was not seen in SWOG 9916 nor in TAX 327. So, there was no significant difference in objective tumor response in those studies.

In summary, we designed this trial to try to stack the deck and find every possible way of causing the drug to progress, and that is what our intent was in designing the trial, something that was clinically relevant.

DR. ECKHARDT: Dr. Brawley?

DR. BRAWLEY: How long has this compound been available? I realize that GPC has only had it for a few years.

DR. ROZENCWEIG: It was introduced into clinical trials in 1992.

DR. BRAWLEY: And you started developing it for prostate cancerB-you got it, number one, and started developing it for prostate cancer when?

DR. ROZENCWEIG: Well, actually, I was responsible for satraplatin with the previous

sponsor so I have bee involved st satraplatin since 1992, including in the development of prostate cancer.

DR. BRAWLEY: I am asking when the GPC started prostate cancer studies.

DR. ROZENCWEIG: This study was started in 2003. The first patient was entered in September, 2003.

DR. BRAWLEY: And you got me to the point where I can make my point to the patient advocate. This drug has been around for 15 or 16 years and it would be nice if drugs like this-Band I wanted to point out that GPC was not the sponsor until very recently, but it would be nice if you put heat on somebody and it not be the FDA to approve it, but it be the companies to develop these drugs faster.

DR. ECKHARDT: Thank you. Dr. Dahut?

DR. DAHUT: I just want to clarify a point you made earlier. You said that if someone progressed concurrently with pain and radiographically you scored it as pain, is that

correct?

DR. ROZENCWEIG: I don't remember having said that but if this is what I said, that is not correct.

DR. DAHUT: That is not correct?

DR. ROZENCWEIG: That is not correct. If a patient had radiographic progression and pain progression at the same time, there was an hierarchy and the patient, for the purpose of the classification by first PFS event, was considered as a radiograph progressor.

DR. DAHUT: So, if they progressed concurrently, it actually was radiographic. I am trying to break up the distribution question, a relatively small percentage progressed by radiographically first, although it still appeared to be significant.

DR. ROZENCWEIG: Very few, yes.

DR. DAHUT: The second question, was any stratification done amongst patients who were entered on trial who were intolerant of prior chemotherapy as opposed to actually progressing on

the prior chemotherapy?

DR. ROZENCWEIG: No, they were required to have documented progression regardless of prior tolerance or intolerance.

DR. DAHUT: So, while on prior the chemotherapy or as opposed to stopping the chemotherapy and then later progressing.

DR. ROZENCWEIG: We have had a mixture of both.

DR. DAHUT: And was there any stratification on that at all?

DR. ROZENCWEIG: You must remember that when we designed the study there was no experience so we really didn't know what were the prognostic factors for these patients, and we discussed with a number of experts and everyone had his own list or her own list of prognostic factors. We picked up the three that we had and we decided that we would do an analysis by the menu that had been, you know, proposed by anyone. This particular aspect was not part of the stratification, the reason being that there was no consensus that PSA increase, or

whatever increase, would really be considered for being the factor. So, we thought that was a little bit too complicated. What I can tell you is that we had this for prior docetaxel. I don't know if that addresses your question. Can I have the slide that we just showed?

DR. ECKHARDT: Briefly, please.

[Slide]

DR. ROZENCWEIG: It shows you the duration of prior docetaxel therapy and the time from docetaxel to randomization into SPARC. So, the duration of docetaxel therapy was 21 months. So, you can infer from this that these patients were roughly refractory, but we can't really answer the question.

DR. DAHUT: Thank you.

Questions to the ODAC and Discussion

DR. ECKHARDT: Thank you. We are going to move on now to the discussion among ODAC and questions, and I would ask that Dr. Pazdur prioritize these.

DR. PAZDUR: Yes, why don't we go to

discuss question two and three together because basically this gets into a reliability issue? One of the things that, you know, we would like to emphasize here which goes back really to this issue of accelerated approval is that for accelerated approval you still need substantial evidence of efficacy here. Okay? It is not a lesser standard. The issue is one of the surrogacy of the endpoint basically, and the issue also is one that we would still want the same robustness and reliance on that point that we are dealing with.

So, I guess I would like some discussion of question two here and three, and then voting on two and three, and then we could go to four.

DR. ECKHARDT: So, we will have our same procedure, starting with Dr. Brawley.

DR. PAZDUR: And discuss two and three together.

DR. ECKHARDT: Two and three, briefly.

DR. BRAWLEY: Briefly, first, I think that this drug clearly has activity in this disease and I would predict that it ultimately will be

approved. However, I would separate accelerated approval from regular approval, and there is a third category, premature approval. And, I think that the answers to both of these questions are no, although I am worried about the radiologist issue. The company did not help me with that. Was pain progression reliably assessed in the trial? Almost is the answer.

So, I was thinking about taxotere when Dr. Petrylak was talking and I would remind the audience that taxotere given weekly versus taxotere given every three weeks had the same PSA response, but the taxotere given every three weeks ultimately was found to have a survival response. So, I would tell the advocates pushing for approval of this drug that you have to learn a little bit about these things. We would be giving taxotere weekly if we had prematurely approved taxotere for prostate cancer without fully understanding it, or understanding it better at least. So, that is my answer.

DR. ECKHARDT: Wait, Dr. Brawley, what was

your specific discussion on number three then?

DR. BRAWLEY: Number three, I think pain was almost adequately assessed but it didn't meet my standard for being adequately assessed.

MS. ECKHARDT: Dr. Perry?

DR. PERRY: Thank you. I don't think the radiologic assessments were reliably assessed, but I think the only way that could be done would be using an odd number of radiologists, less than one or less than three. I think that the more radiologists you get, the more opinions you get and I think that is hopelessly going to confuse things. I think that is seen as a further measure when you have a composite measurement when you are measuring multiple different things, then it adds further to the confusion rather than enlightenment further.

I think that is why I am also a little bit confused about the pain assessment. I would have preferred a straight 1-10, better, worse, etc., rather than the assessment that has been done. So, was pain progression reliably assessed? Probably. I guess if I had to vote I would say yes but it

would be a meek yes.

DR. ECKHARDT: Dr. Richardson?

DR. RICHARDSON: With respect to radiologic progression, I guess I share Dr. Perry's reservations. I think a number of medical oncologists looking at these films might do just as well. With regard to pain progression, I guess I am still troubled by that concept as an endpoint. When you have a group of patients who are asymptomatic or taking minimal amounts of analgesics, to use time to pain progression as some sort of favorable effect I think is pretty distressing and so I don't believe that this was reliably assessed in this trial.

DR. ECKHARDT: Eckhardt. I had concerns about the radiological progression because, as you know, when you are assessing things by RECIST criteria this bone only disease falls into a non-target status. So, when you are looking at responses you actually need to have a primary target with a secondary non-target. So, I was just concerned all along that that would be difficult to

measure and adjudicated. So, I think that is a major concern.

I think with regards to pain progression, you know, I think there is always a dilemma between having a patient who is symptomatic where you are observing for a response and I know, having done studies like this in pancreas cancer, that we hate to actually have the patient be in a certain amount of pain in order to enroll them onto the trial, but I think at the end of the day it is easier to assess a pain response than a time to pain worsening. So, I think some of the concerns about whether it is clinically relevant revolve around the fact that you did have patients who were in the 0 and 1 category that really comprised 60 percent of the population, and what you were looking for was a worsening and, in fact, the question is did you need a cytotoxic therapy to actually palliate that pain. Dr. Wilson?

DR. WILSON: With regard to question two, I too share the other panelists' feelings about this, but ultimately radiographic progression should be a

surrogate for some clinical benefit and, at least from a survival point of view, I think we have yet to see that. I also share some comments that survival benefit may well be seen, but I don't think we see that at the current time.

With regard to question three, I really have major reservations because, to me, that is the major reason to approve the drug at the current time. Not only is the endpoint different from other trials in that they have looked for pain worsening versus pain improvement, but some half of the patients had, quote, pain worsening because they had increased opioid use and that is not a validated endpoint either. So, I am very concerned about question number three and how valid that endpoint is at the current time.

DR. MORTIMER: I have nothing unique to add. I mean, this is the problem with bone only disease and radiographic assessment, and I share Dr. Wilson's concern about the impact of opioids and nonsteroidals on the third question and how that impacts those results.

MR. ANDERSON: Well, as the least qualified of this panel to discuss these things in detail, from a patient's perspective, I have to agree that I do not think the third question has been adequately addressed. It is not telling us what we need to know before we do something.

You know, is it true that what I have seen here is that the SPARC study shows a ten day advantage for satraplatin versus the placebo in median progression-free with little or no increase in overall survival at this time? Is that a true statement?

DR. ECKHARDT: Yes.

MR. ANDERSON: Okay. Well, as a patient rep then, I express deep concern about us suggesting that this group of men who are already besieged by extreme toxic side effects be subjected to more without definite proof that there is a benefit here for them.

DR. HARRINGTON: So, context here is important for me. I guess I don't share the optimism that the survival results will emerge as

positive. They may but they very well may not. So, as a result of Dr. Pazdur's comments that accelerated approval must be based on a robust endpoint if it is different than overall survival, I don't see the robustness. I don't know whether the radiologic assessment was right and I don't know whether the pain assessment assessed pain properly. What I do know is that at least on the pain side there were methodologic flaws that could lead to real lack of reliability of the instrument. In the setting where I need a robust endpoint for accelerated approval I don't see it, I don't see the robustness.

MS. HAYLOCK: I don't have anything to add about the radiologists. I think a two out of three chance of being right is maybe not a good thing.

In regards to the pain issue, first of all, I think it is incredibly exciting that people are looking at pain outside of the context of an isolated symptom because we all acknowledge that pain is a component of a symptom cluster that is being reported quite a lot more in the literature,

although I am not sure that the company really explained well enough why these particular components of that cluster they included because I think pain can be both additive and cumulative in regards to other issues that surround pain. So, I think that there probably could have been a better measure or more reliable tools used to assess the pain.

DR. FARRAR: So, I agree with the concerns about question two, but would argue they don't matter with regards to the outcome as long as they were not applied differentially to one group compared to the other. As long as the problems existed in both groups, then you might miss a good outcome but it is going to tend to push the result towards the null.

The same I think applies to the validity of the measurement in question three. My concern is more along the following lines, which is that the difference that we see between the groups is very small. Given the toxicity of the treatment, if this were a drug that we are trying for approval

for pain, I would argue that the benefits don't outweigh the risks. In addition to which, a question was raised about the potential for blinding. We know that patients who suffer side effects have a bigger placebo effect with regards to pain. It is well demonstrated. If you give a person a shot they have a bigger placebo effect than if you give them a pill. Given the fact that there were high rates of serious side effects in the treated group, I would argue that the entire pain benefit could be explained potentially by patients experiencing that and having a placebo effect, placebo being their brain takes over and controls their painB-a great thing; I wish I knew how to use it. So, I would argue that the issue was not so much the measurement, it is that there is a real problem here as to whether this pain is adequate and I would argue that if there were not a survival difference I wouldn't want this to treat patients with pain.

DR. DAHUT: My perspective may be a little bit different, and I do want to commend the

sponsors on some extent in trying to do what they are doing clinically and put in an objective measure. It is so hard in prostate cancer to come up with something that you can answer without survival, particularly in a population like this. So, you know, a response in tumor, and we used PSA for about five or six years and we have moved away from that because we would probably stop patients who were responding based on PSA too soon and vice versa.

So, as far as the radiologic opinion, I don't have a great concern with it because I think, once again, you would have the same sort of error on both sides and these bone scans are incredibly difficult to interpret, and if you get two that agree it should work its way out in a randomized, blinded trial when you have independent radiologists. So, I think that should balance one way or another.

I think the pain assessment is complicated and I think attempts were made to sort of put in an objective measure what we do in practice. You

know, if pain is getting worse, you are losing weight, stop the treatment and do something else. So, there are problems I think in all the measures here. I think there is probably some benefit. Again, you have independent reviewers looking at these forms, who are blinded to what they are on, but there are obviously a lot of intangibles such as the fact that people have toxicities, and such.

So, I am not bothered particularly by the problems of radiology. These bone scans are hard to interpret and if you have two out of three that agreed, that is probably good enough for me in a blinded trial.

I think on the pain progression I am sort of in that meek agreement that it is probably reliably assessed. It is probably not the way we would do it in real life but it is a noble attempt. It probably falls a little bit short.

DR. KRASNOW: I share the concerns about the radiologic assessment, but I also agree with some of my colleagues that it is a lesser concern in the context of this trial because of the

randomization and the way that these studies were analyzed in a blinded fashion.

I am a lot more concerned about the pain endpoint and, in particular, I am very concerned that this was not truly a blinded trial because although the patients were blinded to their treatment assignments, not only might they suspect their assignment by symptoms, but they also probably had access to their CBC results. If they know that their white count is 2, they could guess what they are getting. And, I think it is axiomatic that you do not use a subjective endpoint in an unblinded trial and I think that this, to me, is a major issue. There are all the other concerns about the pain endpoint but I think, to me, this is a serious one. It is a mistake that has been made in other settings recently with other drugs and I think it applies here too. This is a subjective endpoint and an unblinded trial.

DR. ECKHARDT: Thank you. Now we need to take our vote on these two? No?

DR. PAZDUR: Let us do this--

DR. ECKHARDT: You keep changing things.

DR. PAZDUR: Because we are sensitive to people's time and we have heard the comments here. Why don't we go to four? Basically, we realize that there is a discrepancy between what the sponsor had told us on one occasion and what they are saying now as far as when the mature survival data is going to be available. But what we really are asking the committee is should we defer consideration of accelerated approval, especially in consideration with all of these comments that have been made, and really wait for the overall survival? And maybe we could just go to a vote on that question.

DR. ECKHARDT: So, the plan is to do a hand-raise vote for question number four. Let's discuss first, starting with Dr. Brawley.

DR. BRAWLEY: Without a survival endpoint, I am not certain that satraplatin is better than narcotics in the treatment of pain and quality of life in these patients. So, I think we do need to have a survival endpoint. I do believe satraplatin

will meet that survival endpoint but I think we need to have it.

DR. PAZDUR: The question posed is should we wait, and your answer is yes?

DR. BRAWLEY: Yes.

DR. PERRY: Perry, yes.

DR. RICHARDSON: Richardson, I don't share Dr. Brawley's enthusiasm. Nevertheless, my answer to this is yes.

DR. ECKHARDT: Eckhardt, yes. I think that without that it is hard to look at some of the issues with regards to pain as a truly palliative therapy and I think that is sort of what you would be left with.

DR. WILSON: Yes, I think we should defer until the survival data is out.

DR. MORTIMER: Yes, although I am not optimistic that there will be survival. It seems to me like Tarceva where we have a ten-day progression-free survival but perhaps no impact on survival.

MR. ANDERSON: I vote yes.

DR. HARRINGTON: Harrington, yes, to wait.

MS. HAYLOCK: Haylock, yes.

DR. FARRAR: John Farrar, I want to commend the sponsor for putting in a measure in attempting to do this. I would strongly encourage others to consider how to do this and to talk to Dr. Cleeland first rather than second. But I have to vote yes for this.

DR. DAHUT: I guess I am the Brawley surrogate here, but I believe this drug is better than placebo. However, I do vote yes on this.

DR. KRASNOW: Krasnow, yes.

DR. ECKHARDT: Do you want us to continue on with question one?

DR. PAZDUR: It is not necessary.

DR. ECKHARDT: All right, then I would like to thank everybody for their participation. We will now conclude.

[Whereupon, at 4:45 p.m., the proceedings were adjourned.]

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