

Comprehensive Cancer Care: Integrating Complementary & Alternative Therapies
Antineoplastons

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Session 305: June 13, 1998

Dr. Burzynski: Thank you very much, Ralph. I appreciate your support. Without you, I would never be here. Probably I would be enjoying Camp Fed somewhere. Fortunately I can talk to you today.

Let's start with the first slide. Cancer originates from abnormalities of two different types of genes. We have abnormality of oncogenes, which are accelerators of the cancer process, and then we have abnormality of tumor suppressor genes, which are cancer brakes. In order to successfully create cancer, we need to push the accelerator switch on and to turn off the brakes. Then we can have cancer. A logical approach to control cancer should go in reverse. We should turn off accelerators of oncogenes and turn on brakes of tumor suppressor genes. Then perhaps we can get rid of cancer. That's exactly in a few words the mechanism of action of antineoplastons.

Antineoplastons are simple chemicals. They are amino acid derivatives, peptides and certain organic acids. They exist in our body. You can find them in the blood, in various organs, and also in the urine. Initially they were isolated from blood, then from urine, and ultimately we have made them through chemical synthesis. Since 1980 we are concentrating on synthetic antineoplastons, most of the time on antineoplastons A10, AS2-1, and AS-5. These antineoplastons work as chemical micro switches. Based on the research conducted all over the world by numerous researchers, including the scientists of the National Cancer Institute, we

know now that antineoplastons can turn off the signal which is coming from oncogenes, especially from the ras oncogene family, and can activate tumor suppressor gene p53.

The ras oncogene family is perhaps the most important among oncogenes. It is responsible for approximately 40% of all cancers. The signal which is transduced through ras oncogenes comes from the outside of the cell. This is usually the signal which is coming from growth factors. Growth factors are docking on the growth factor receptors on the cellular membrane, and from this point we have a cascade of events. We have numerous steps through which the signal is being transmitted. The signal travels along the cellular membrane and finally enters the nucleus, where it delivers the message to the cell to multiply. Of course this is shown in great approximation. This is a very complex pathway. We don't have enough time to go into details. I can discuss this later if someone is interested.

In the center of this complex transmission pathway we have protein p21, which is the product of ras oncogenes. This protein is born inactive. In order to transmit the signals it should undergo three different reactions – farnesylation, proteolysis and finally methylation of the protein. Without these reactions, protein p21 will not attach to the membrane (as I mentioned, the signal travels along the membrane), and the signal will not be transmitted.

Antineoplastons AS2-1 and AS-5 control two of these reactions, farnesylation and methylation. When we apply this to the patient who has hyperactive ras oncogenes, then the signal from the oncogene is turned off. Antineoplastons will not allow protein p21 to mature. Then malignant cells will stop multiplying. This is only a partial victory, because they can persist in the body. When the time is right, they can multiply again. In this respect we have to use another switch, the tumor suppressor gene switch, which should force these cells to undergo programmed cell death. Gene p53 is the guardian of the quality control of the cells. It forces

malignant cells to die through apoptosis or programmed cell death, or in other words, to commit suicide.

Gene p53 is abnormal in approximately 50% of all cancers. It is abnormal not necessarily through mutation. According to recent studies, and the article which was published in *Science* magazine at the end of last year, in about 50% of cases gene p53 is chemically blocked. If we learn how to unblock it, we can use the gene which is in our body. Gene p53 is responsible for synthesis of protein p53. Protein p53 works through a very complex biochemical pathway. Again, there is not time to go into details. But I'd like to mention that protein p53 transactivates another gene which is called WAF1. When this gene is activated it's responsible for the synthesis of protein p21^{WAF1}. It's a complex name. Again, we have p21, but this is a completely different protein which I mentioned before, p21^{ras}. Protein p21^{ras}, p21^{WAF1}, is responsible for unblocking the tumor suppressor genes which have been blocked chemically before.

As I mentioned, in a number of cases of cancer the gene initially is not mutated, but it is blocked. It is blocked through attachment of simple chemical group. When certain sequences of the gene, called promotor sequences, are excessively methylated, then it's not active. It's like coated with paint, or some other coat, which will not allow the gene to express its activity. CH₃ groups, or methyl groups, are attached to cytosine residue of the gene. This reaction is controlled with the enzyme called methyltransferase. Again, this enzyme is initially inactive. In order to do the job, block the gene, it should be activated through attachment to protein PCNA. Protein PCNA, when it's attached to methyltransferase, will cause promotor sequences of the gene to be methylated or blocked. But protein p21^{WAF} will prevent this reaction, because it will bind protein PCNA. As a result we have the tumor suppressor gene unblocked.

This means that, if I can reconstruct what happens, protein p53 activates gene WAF1. Gene WAF1 is responsible for making protein p21, and protein p21 will cause the genes to be unblocked. We are talking especially about gene p53, but we have some indication that some other genes, such as neurofibromatosis 1 and 2 and VHL genes, also are unblocked through this particular reaction.

Antineoplastons AS2-1 and AS-5 activate gene WAF1. They are bypassing gene p53. They directly activate gene WAF1 and cause production of p21^{WAF}. Then this protein will unblock tumor suppressor genes, and tumor suppressor genes will do their job. They will force malignant cells to die through apoptosis or programmed cell death.

Basically I'm talking about a new approach to gene therapy. Until now, gene therapy consisted of introduction of the gene from the outside of the body by using various vector viruses. This is very complex. The method consisted either of replacement of mutated or deleted genes or introduction of tumor suppressor genes. Here we are talking about a different approach. We are using molecular switches, simple chemicals which can turn off genes which are accelerators of the cancer process and turn on the genes which are the suppressors of the cancer process. If we do both of these things, we can get rid of cancer. This is true of the cancers which have involvement of these two genes. There are many other cancers which have involvement of different genes. Then the cancer requires different switches.

Antineoplastons have been discovered a long time before these genes have been discovered. The discovery of antineoplastons occurred about 30 years ago. Ten years after that we knew about first oncogenes, and another ten years after that about tumor suppressor genes. In science this is not unusual. The first use of electrical energy on a large scale was introduced

as we know by Thomas Alva Edison, but the use of electrical energy would not be possible if we did not have the switches which control the use of energy. Switches in this also were discovered many years before by a scientist probably few know, Alessandro Volta. Without the switches we would not be able to control the energy. We hope by using these simple switches named antineoplastons we'll be able to control cancer.

Research done all over the world proves that this is the right idea. A number of important studies have been done by the scientists from the National Cancer Institute. We really don't have any doubt that that's the mechanism of action of antineoplastons AS2-1 and AS-5. Antineoplastons went through numerous preclinical studies, in the laboratory, in mice, etc. After that they entered into Phase I studies. From all of these studies we knew that they can produce marked inhibition of cancer growth, both in the laboratory and in patients. They are practically nontoxic.

The next step was to have Phase II studies, in order to provide how they work in each type of cancer. In this respect we have 72 Phase II clinical trials which are currently done under control of FDA and which are sponsored by our institute. In addition there are two clinical trials conducted by the Japanese medical school under the control of the Japanese government. The studies which are sponsored by our institute have a few things in common. The design is common for most of these studies. It is required to treat approximately 40 patients. Of course, since we have 72 trials, we are talking about different projects for pancreatic cancer, different projects for cancer of the esophagus, different projects for lung cancer, etc. Almost all cancers except those which respond to chemotherapy are covered in this large project.

If after treatment of 40 patients in each of these studies, we come to the conclusion at least four patients have either complete disappearance of the tumor or more than 50% decrease

of the tumor size, then in the eyes of FDA we've proved the point that there is some antitumor activity. Of course, many patients who are involved in these trial have less than 50% decrease of the tumor size. They live comfortably for many years despite the fact that they still have the tumor.

This is especially important for bad cancers like highly malignant brain tumors or pancreatic cancers. Until now, FDA disregards these cases. But most of the scientists who are involved in clinical trials see stable disease cases (less than 50% decrease of the tumor size and less progression) as responses. They are now forcing FDA to change their stance. They feel that these stable disease cases are important and also should be accounted for as responses.

Another common feature for these trials is that these patients are basically hopeless. We are limited by FDA to the treatment of the toughest cases you can get. They come to us highly recommended and with very good past history, usually seen in the best places in the country or the world. The main common feature for them is that many of them are adults they turn away because there's nothing else can be done. In some of these cancers FDA does not allow us to treat patients unless the patient had failure on two different types of chemotherapy. All of these patients have widely spread disease and many of them are close to death. We are glad to help these patients, but of course it is a tough thing to treat these patients.

Another feature is that we enjoy, or sometimes do not enjoy, very good care of federal government. FDA is supervising us so closely that within the last two years we sent 1,020 letters to FDA, an average of 1.5 letters a day or more. We don't mind. We are reporting to FDA sometimes every day, sometimes every week, and of course we are sending monthly and annual reports. This helps us to do everything close to perfectly because we are not forgiven the smallest mistake. There was a time when I believe FDA had 50 people in their task force trying

to find out what is wrong in our studies. Some of these letters, together with attachments, have from 1,000 to 2,000 pages. But we can do it. We increase our staff, and we can live with it.

The other feature of this is that FDA required for most of these patients in clinical trials, especially those who are taking slightly higher doses of antineoplastons, to have a local co-investigator. That is a medical doctor experienced in the treatment of cancer who will be registered with FDA as co-investigator. Initially it was nuisance. We need to ask the doctor to fill out the forms, to be involved with that, and some of them don't like FDA. We are approaching around 800 investigators.

But this means that we are not alone. We have numerous doctors all over this country, all over the world, who are working with us. Then our successful cases of cancer are strictly reviewed by top outside consultants. We send our slides, our film, to the top people in the country to make sure that what we do is right, that our response is right, that our diagnosis is also right.

One clinical trial out of these 72 is somewhat different. About two years ago FDA had the idea that all of the patients who are treated in our clinic outside clinical trials should be grouped together in one protocol called CAN-1 in order to continue the treatment. This means that whoever wanted to take treatment should be in clinical trial, and who did not wish to do it should stop the treatment. This resulted in a large group of patients in the trial. In protocol CAN-1 we have about 133 patients who have one common feature. Previously they were treated with antineoplastons.

According to orders from FDA, we grouped them in one large clinical trial. We divided these people into six different cohorts based on different diagnoses. The most numerable cohort of these people were those suffering from brain tumors. Since the beginning of our clinical trials

we concentrated on the treatment of primary malignant brain tumors, mainly because these tumors are uniformly bad. They are usually deadly. They carry very bad prognosis. We felt that if we proved that we can successfully treat such patients, then perhaps this would convince the skeptics.

We have 43 patients enrolled in our first trial in brain tumors on the protocol CAN-1. A few years ago when FDA decided to open this CAN-1 protocol, we had 66 cases of primary malignant brain tumor. Forty-three of these patients decided to be enrolled in clinical trial. In order to prove that there is no bias in selection of these patients, we started also the group of patients who were not admitted to the trial.

This was the decision of the patient, whether to be in the trial or not. Some simply did not want to be in a clinical trial, and they were not involved. If you compare demographics of the patients who were not admitted and the patients who were admitted and outcome, the responses of patients, we don't see a significant difference. If you would add all of these patients together you would come up pretty much with the same result.

I would like to tell you about the results. 44.5% of these patients have complete and partial responses. 33.3% have stable disease, and only 22.2% of patients progressed. The most numerable group among these patients were those suffering from glioblastoma multiforme. The second largest group were those suffering from anaplastic glioma. Both of these categories obviously carry dismal prognosis. A small percent of patients suffered from low grade astrocytoma and some other tumors. What is important in this study is that we are talking not only about remarkable responses, but also we are talking about increased survival of these patients.

Here's a diagram which shows the survival of the patients. Each of these patients who responded to treatment is represented by a different bar. The height of the bar corresponds to years of survival. For some of these patients we are reaching now over 12 years survival since the tumor diagnosis, and over ten years survival since they came to us for the treatment. When they came to us, usually they carried only two months of life expectancy. If we compare mean survival time with the other treatment, we are about three times better than the other treatment. I believe it can get only better, because there is no indication that these people will die. They are free from tumor. Hopefully they will live happy ever after.

This was the first trial which was somewhat unusual because this was a retrospective trial. We used patients who were already treated before with antineoplastons. This is the trial where we have the longest supervision of these patients. We have people with glioblastoma multiforme who are now over five years since we treated them and six years from the time of diagnosis. This is unheard of in medical practice. Usually these people have a life expectancy of six to nine months. We have three additional clinical trials which reached the final point. In these trials we did not have necessarily 40 patients enrolled, but in them we could see four cases of complete and partial response before 40 cases enrolled.

This is an example of another trial, Protocol BT-9, dealing mostly with astrocytoma. Here we had only 11 patients accrued, and we obtained 62.5% partial response. This trial opened not even a year and a half ago. Two of these partial responders are now approaching complete response. In addition we have 25% with stable disease, and only 12.5% progression.

We now have six Phase II clinical trials which have reached conclusion. In these trials we have altogether 107 evaluable patients. Some of them are suffering from astrocytoma, some from brain stem glioma, and another category is mixed glioma. In Protocol CAN-1, as I

mentioned, we have a substantial percentage of glioblastoma multiforme. In all of these 107 patients we got 37% of complete and partial responses. We have 36% of stable disease and 24% of progressive disease. Of course, this is a small segment of our clinical trials.

We are conducting altogether 24 different clinical trials in various types of brain tumors. In all of these we have close to 200 patients enrolled. If we look into statistics of these trials which are not yet finished, again we come up with approximately 37 or 38% of patients who have glioblastoma multiforme, about 33% of patients who have malignant astrocytoma, and about 10% of patients who have brain stem glioma. Then we have some other categories of relatively rare brain tumors. Practically every type of brain tumor is represented here. Again, we see a similar ratio of responses. The rough estimation is that approximately one-third of the patients are failures, approximately one-third are complete and partial responders, and one-third are stable disease cases. We believe that at least in brain tumors, we proved the point that the treatment has activity against cancer.

We continue to do about 70 other clinical trials in various indications. We see some exciting results, but also failures. It's obvious that in some of these trials you are not going to have any good responses, but in some others perhaps we get something very interesting. Ultimately we hope that this should convince FDA that this treatment should be finally approved and used by every doctor. In finishing this presentation I would like to thank our colleagues here at this table and Dr. Ralph Moss and all of you for attending this conference. I hope you find it interesting. Thank you very much.

Dr. Moss: Thank you very much, Dr. Burzynski. Our next speaker will be Li-Chuan Chen. He is a 1991 graduate of the Toxicology Program of the University of Kentucky, with a

fellowship from the National Cancer Institute and complete postdoctoral training on chemoprevention of retinoic acid and beta carotene. In 1994 he moved to NCI laboratories to continue his research on the mechanism of action of phenylacetate, the major ingredient of antineoplaston AS2-1. Dr. Wayne Jonas, Director of the NIH Office of Alternative Medicine, then recruited him to evaluate the science of all antineoplastons under a professional service contract in 1996. Dr. Chen also conducted an evaluation on Cone metabolic chemotherapy. His research led him to take an interest in many modalities of alternative medicine. He is a practitioner of HoChi, a special form of Chinese Qi Gong exercise, and he continues to investigate alternative cancer therapies and work collaboratively with other alternative medical practitioners in the foothills of South Carolina. Dr. Chen.

Dr. Chen: Thank you for the introduction. Talking about science you cannot leave politics and economics behind. Today I'm going to talk about the science of antineoplastons from three perspectives – historical, and the perspective of conventional medicine and also holistic medicine. Before I go further with my talk I'm going to define antineoplastons better. Dr. Burzynski talked about antineoplastons AS-2-1 and A-10, but initially antineoplastons started with A and then divided from A-1 to A-5. A-10 and AS2-1 are actually from antineoplaston A2 fraction.

Antineoplastons first came out of urine extract, and I'm going to talk about what's in urine therapy. There's a long history of using urine. It's not just about drinking urine. It's modifying your life style and drinking urine. There's a long history for health prevention and even disease treatment. That even started from Greek times. More recently the Japanese military doctors ran out of antibiotics during World War II and asked the soldiers to use urine to

wash the wounds. The soldiers recovered from infections miraculously. So there's something in the urine. There is a lot of literature in Chinese about the therapeutic use of urine drinking. Similarly, there are English publications, a Dutch one, and an American version. These are the literature publicized in alternative medicine.

There is also a history of urine therapy for cancer. In 1982, a doctor by the name of Nathan Sloane isolated another entire antineoplastic protein from urine. The fraction of urine that he used actually is the part that Dr. Burzynski throws away in his urine extract. In 1995, Dr. Ming Chen Lian, a Taiwanese, published his clinical results. There are two clinical trial results in the web site of the Chinese Association of Urine Therapy (<http://www.auto-urine.com/english.htm>) He has purified another compound called CDA-II, and it is showing some positive effect in treating cancer. The point is there's a long history of using urine drinking or even urine extract for therapeutic purposes. Dr. Burzynski is part of the tradition. That's my first point, from the historical perspective.

In 1996, I was recruited by Dr. Wayne Jonas to do an evaluation of all the antineoplastons, the result of which is a 200-page document. Obviously I'm not going to talk about it all. The text is 81 pages long and single-spaced. If you'd like to read it, give them a call to obtain the whole document. I even wrote a manuscript, but it has never published. Or I never got any word about it after completing my contract.

Dr. Burzynski's publications have some flaws which are commonly made by other scientists. I'm not going to comment on this too much. My method of evaluating his data is quite simple. I reviewed all the literature available to me, peer-reviewed articles or non peer-reviewed articles. I also looked at the publications by others who happen to have data to support

his theory or his claims. In addition, I did some laboratory work to show the anticancer effect of certain compounds. I will present some of those data.

In 1990, the U.S. Government published the OTA report on unconventional cancer therapy. In that publication there's a section in which some oncologists have commented on Dr. Burzynski's publications and the real data. I went back and read the literature. I took out some of the data points these oncologists have questioned and recalculated the response rates. That's another way I evaluated his publications. With thorough investigation, my finding is that there is not a thread of falsehood or fraudulent claims in his publications. He's like any other clinician trying to publish things with mistakes. But those mistakes are not great enough to discredit him, as others would like you to believe. I continue to compile things like this with preclinical data and clinical data. Here are the laboratory data, which further support his theory and claims.

I didn't know Burzynski before writing the evaluation. I wanted to make sure that I was not getting myself involved in the controversial issues. I did some study and tried to verify certain claims that he has. For example, phenylacetate is proclaimed by the conventional medical establishment as the active ingredient of AS2-1. The other inactive ingredient is phenylacetylglutamine. However, in my studies I have found that in the presence of phenylacetylglutamine the effect of phenylacetate is enhanced. They have either an additive or synergistic effect in killing cancer cells in vitro. For years Dr. Burzynski has been saying that those two compounds have interactions, but the conventional medical establishment doesn't take his words. My results support his claim.

After I got that result, I told Dr. Moss. Dr. Moss told Dr. Burzynski, and Dr. Burzynski called me. They also informed me that phenylacetylglutamine by itself has antitumor effect. I said, "That's great. Let's go back to the lab and do some work." The results show that

phenylacetylglutamine at more than 10 mM inhibits tumor cell growth in the petri dish. At that moment I realized that what he has been saying has been true for years. Phenylacetylglutamine has anticancer effects, albeit in much higher concentrations.

Some of Dr. Burzynski's clinical findings have been partially confirmed by other clinicians around the world, including a study in the Netherlands, several studies in Japan and Dr. Lian's studies. From phenylacetate more than two dozen analogs in the organic fatty acid group have been found to have anticancer activity in vitro. I looked at some other compounds too. From Dr. Burzynski's research actually one can further the whole field to include three groups of antitumor compounds – organic fatty acids, amino acid derivatives and some of the piperidinedione compounds. Phenylacetate and phenylbutyrate belong to organic fatty acids, phenylacetylglutamine is an amino acid derivative and antineoplaston A10 is a piperidinedione.

Dr. Ming Chen Lian left Dr. Burzynski in 1992 and went back to Taiwan. He further purified compounds out of urine extract. One compound called CDA-II has been put in clinical trials, one in China, where Dr. Burzynski has no patent rights on any antineoplastons, and another one in Japan. The first study showed that the CDA-II compound had some effect on tumors. Complete remission and partial remission is about 25%, not as great as Dr. Burzynski has shown you of the 45% that he is getting. There's very little adverse effect with CDA-II compound. The second study is conducted with Dr. Sano in Japan. He used CDA-II compound and vitamin C. This study apparently has a better response rate. The partial remission is 34% and complete remission is about 9%, so it's about 43% with complete and partial remission combined.

In the orthodox medical communities researchers have studied phenylacetate's antitumor effects. They have conducted several Phase I studies and perhaps, by now, more Phase II

studies. One study is a Phase II phenylacetate for glioma treatment study, of which four out of 19 patients have some responses to it. That's published by Dr. Michael Prados in 1996 in the form of an abstract.

The following table summarizes my evaluation of Dr. Burzynski's antineoplastons. Some of the compounds have evidence to support antitumor effect in vitro and in vivo. On the right-hand side is the clinical effect of these compounds. I have parentheses over it basically saying that it needs further confirmation by independent investigators, but as you can see there are many positive (+) signs on the table. The more positive signs, the more evidence there is for anticancer effect in each category: in vitro anticancer activity, differentiation induction, in vivo anticancer effect, or chemoprevention and chemotherapy.

I have evaluated the scientific validity of antineoplastons. Next I look at the theoretical basis of antineoplastons. Dr. Burzynski proposed that antineoplastons are a biochemical defense mechanism against cancer. He hypothesized urine extracts of antineoplastons can normalize the plasma level of these antitumor peptides and other anticancer compounds.

In 1995, I stumbled on a paper by a Hungarian scientist. He started out from a different point. He used epidemiological studies and figured out some of the nutrients that supposedly would be beneficial to cancer patients. He put all these compounds together in a mixture and found that mixture has anticancer activity in animal model. He proposed a mechanism called passive anticancer defense mechanism. It's passive because it basically consists of nutrients, not peptides or proteins. His research is heading toward the same direction as antineoplastons.

Over the years, Dr. Burzynski's theories of antineoplastons have evolved. Peptides are ideal compounds as information carrying molecules to normalize neoplastic cancers. In 1986, when he found out some of the amino acids in his extract, the theory has changed and was

modified. As it stands in 1995, peptides, amino acid derivatives, and organic acids are part of antineoplastons that can normalize neoplastic cells. As more and more of these compounds are identified in urine extract, we will know more about what antineoplastons are and how they function in humans.

My third perspective is from holistic medicine. In conventional medicine we see the human body as a mechanical complex. If one part is bad, you cut it out or replace it. If not, live without it. In holistic medicine you see the person as a whole. Based on the homeopathic idea of disease, a disease is the adaptive efforts of the whole organism. Therefore, cancer is the manifestation of adaptive effort to multiple causes. Indeed, literature from both conventional medicine and alternative medicine are converging on the possible causes or risk factors of cancer. There are two opposite approaches of cancer treatment in holistic medicine – either by normalizing the body terrain to inhibit cancer or by identifying the risk factors and causes and trying to eliminate those. Dr. Josef Issels combines both approaches.

These are the three schools for which I combed through the literature in alternative medicine and tried to come up with a unified theory and develop a treatment scheme. It is in that context that I evaluate Dr. Burzynski's antineoplastons in this third perspective. The alternative medicine community proposes there are microorganisms that can cause chronic degenerative diseases, including cancer. Here is a table from conventional medical literature proposing the infections and conditions that could cause human cancer, which in some way is similar to the previous figure you see from alternative medical literature.

There is no evidence to support that antineoplastons have any effect on microorganisms so far, because nobody has evaluated what the synthetic antineoplastons do against those microorganisms and cancer risk factors and causes. Nevertheless, the earlier antineoplastons are

holistic treatment in nature, especially with antineoplaston A. Dr. Burzynski proposed that these antineoplastons could normalize human cancer patients because these are the things missing out from their bodies (terrain). Dr. Emanuel Revici, another alternative cancer doctor, also tried to normalize the body terrain without identifying the causes. In some ways they are similar in approach to treating cancer.

Finally, antineoplaston therapy is part of a long tradition of urine therapy. From the conventional medicine point of view you have seen that there's a certain clinical usefulness of synthetic antineoplastons in treating certain cancers. There's also scientific validity to support the clinical results. The theoretical basis of using just the synthetic antineoplastons is too early to draw any conclusions, but there are several kinds of evidence pointing to the direction Dr. Burzynski has been proposing. From the alternative perspective I would like to say the synthetic antineoplaston is not a holistic practice. It fell into that category simply by default. The earlier version of antineoplaston that's a mixture of multiple compounds, including some that we don't know, is closer to alternative cancer therapy from the perspective of the whole organism.

Dr. Moss: Thank you very much, Li-Chuan. Our next speaker is going to be Dr. Dieter Schellinger. I ask all speakers to please condense and limit your remarks. We have an exceptionally large panel today and we need to have real concise statements.

Dr. Schellinger: My name is Dieter Schellinger. I'm a neuroradiologist. You don't find me in the book because I did not submit a CV. I forgot. I'm an academic neuroradiologist working at Georgetown for some years. Neuroradiologists are neuroimagers. We look at two cross sectional images. Among other things we look at CT and MRI. Every day we make a

neurodiagnosis based on what we are seeing on these images. Therefore we are very much attuned to diagnosing brain tumors, and also following success of therapy with brain tumors.

In the past 15 months we had the opportunity to review MR imaging series of a selected group of patients with brain tumors who were treated with antineoplastons and gauge their treatment response. These patients were selected by the Burzynski Research Institute and were rated by them as patients who showed complete or partial treatment response. We studied a total of 39 patients with a total of 318 MRIs and 939 months of follow-up. We studied these 39 patients over a prolonged period of time, all patients who were treated by the Burzynski Cancer Institute with antineoplastons. The average follow-up was two years. The average number of follow-up MRIs was eight per patient. The image analysis that we conducted consisted of a baseline study which was usually taken at the time of treatment commencement or shortly before that.

The treatment response was measured as shown here. This is actually what the Burzynski Institute gave me for analysis. This is also what NIH uses for gauging treatment response. A complete response to treatment is if there is complete absence of enhanced tumor by MRI lasting more than four weeks. A partial response is if there is more than 50% reduction of enhanced tumor by MRI or less than 100% reduction over a period of more than four weeks. Stable disease is disease that is less than 50% progression, or less than 50% reduction of enhanced tumor lasting 12 weeks. Progressive disease is disease that shows more than 50% progression of enhanced tumor by MRI with no time limitation.

Dr. Burzynski sent me initially these 15 patients of the CAN series, which consisted of a mix-up of tumors, all cerebral pathologies. The treatment assessment by the Burzynski Institute was as shown here in the brackets. CR stands for complete response, PR stands for partial

response. My role was to act as auditor, look at this almost blindly, disregard diagnosis, disregard treatment, if you can do that. There is a great deal of conformity. I downgraded two patients in this series, and I upgraded one patient.

The next group of patients consisted of two major categories, a shorter group incidentally. The first 12 patients are anaplastic astrocytomas, and the group here are mixed gliomas. Once again the assessment by the Burzynski Institute is shown in brackets. You see PRs, you see CRs, and you see there was total conformity as far as our analysis was concerned. The last group of patients consisted of patients who were derived from a number of protocols from the Burzynski Institute, B-8, B-9, B-11, B-15, B-17 protocols, with the diagnosis as shown here. Once again you see the treatment response as gauged by Dr. Burzynski and his associates and you see my analysis. Once again there is great conformity in most cases except for three where I downgraded. In one case I think there is an upgrade. I wasn't sure because I could not follow this case long enough to verify complete response. It will be PR as judged by the Burzynski Institute.

Now let me show you a series of patients. This first patient is a 14-year-old patient with astrocytoma grade III. Treatment start is shown here. The last follow-up MRI is not entirely correct. I followed this later until 1998, so it's two years later than that. The initial response was stable disease as indicated by SD. Then we go to partial response, and then there is sustained partial response. The last phase, not shown here on this slide, between 1996 and 1998, showed complete response.

For those of you who are not used to looking at MRIs, this is a cross section of the brain, looking upwards as if you stand at the foot end of the face and look up. This is left; this is right. What's bright here is a fairly large enhancing tumor. It enhances homogeneously. This is the

medial temporal lobe; this is the inferior frontal lobe; and this is the disease process that we are monitoring here.

Roughly two-and-a-half years later you see that this tumor is no longer enhancing. Little spots of enhancement are still shown, but by and large the massive tumor that you saw before has melted away. That was two-and-a-half years after treatment commencement.

Approximately three-and-a-half years later we see no enhancement any more. By NIH standards this is a complete response. The next slide is four years after commencement of treatment. This is with contact enhancement. This is where we showed the tumor initially. There is no tumor evident in this patient.

The next patient I'm showing you is medulloblastoma in a four-year-old male. Treatments start as indicated. Last follow-up is 1997, not 1996. I had some follow-up images later on. This is the tumor, and this is the fourth ventricle. This is a fairly large tumor that pushes upon this ventricle. Four months later the tumor is gone. This entire mass has disappeared. Three-and-a-half years later, just to see whether this is still suppressed, you see there is still no tumor. This is the fourth ventricle. This large tumor is no longer shown. This is a complete response to treatment.

The next patient is an anaplastic astrocytoma in a 53-year-old male. There was some treatment with radiation therapy in 1949, and also some chemotherapy. But prior to coming to the Burzynski Institute, this patient showed on MRI further tumor progression. Therefore, I suppose, the trip to Houston, and the treatment starts here in mid-year 1995. Last follow-up is as stated here in 1996. Here are the images. Remember, this patient was treated before and the tumor came back. Here I saw a ring-like structure of enhancement and some small parts that are also enhancing. This is a neoplasia. This is a brain tumor. In follow-up images some two or

three months later you still see this lesion, but there is a little bit of a change. Some two months after that it's totally gone. The enhancing lesion that you saw is no longer in evidence. Another sequence approximately half a year after this shows again no tumor in evidence. Again, this was a total response.

The next patient is an anaplastic astrocytoma in a ten-year-old. Hypothalamus, at the base of the brain. Anaplastic astrocytomas are fairly aggressive tumors. This patient had various things done to him. Biopsies showed glioblastoma which is even more than that, but I guess it was restaged later on. This patient began treatment in 1991. The main lesion that is obvious is a huge tumor at the base of the brain in the hypothalamus. On follow-up seven months later it is gone. Images don't lie, so to that extent I can trust what I'm seeing here. In another follow-up study two-and-a-half years after commencement of treatment, once again this lesion which was huge and was seated in this location is no longer in evidence.

The next patient is anaplastic astrocytoma, again a fairly aggressive tumor of the brain stem. Here we take a biopsy for diagnosis. The follow-up went beyond 1996 into 1998. Here's the lesion. The lesion is quite obvious once you see it. This is again the fourth ventricle being distorted, partly compressed. This is now looking not in the actual plane but as if you stood in front of the patient. This is what we call a coronal plane. Again this is the fourth ventricle here; this is the tumor. You see how the fourth ventricle is being displaced to the side. Five months after treatment this thing is still there but looks a little smaller.

Three years later, the mass is gone. This is going back to the actual images Remember, there was a mass here that distorted this. The next slide portrays what happened ten years after beginning of the treatment. The mass is gone entirely. We see a little dot of scar. This is where

the mass started. Now you see what we call a focal area of encephalomalacic which is the only evidence of something having been there some time ago.

I have two more cases to show you. One is a mixed glioma in a 23-year-old. This patient I know myself. This patient is a young physician who was diagnosed who has a mixed glioma grade 2 to 3. He had a subtotal tumor resection. He had some chemotherapy in 1996. The Burzynski treatment started in March. Last follow-up was not in 1996, but 1998. This is how it looked after he came to Dr. Burzynski with part of the tumor taken out. Once again, this is a coronal cut. This is the skull on top; this is the scalp subtissue; and here is the enhancement. This is the rind of the tumor that's left behind. There is some tumor probably taken out, but this is what we are concerned about. This we know is abnormal tissue.

Four months after this treatment has begun this rim of enhancement is significantly smaller. At nine months after the commencement of treatment there is no longer enhancement, at least not obvious. There may be a little enhancement over there. This hole is getting larger because the space expands into the territory previously occupied by this neoplastic tumor. This is now ten months. Again you recognize the lesion there, a little residual enhancement. Now, at two-and-a-half years after commencement of treatment, it looks like this. There is no more enhancement. There is just a big hole.

The last patient is a multiforme glioblastoma. Multiforme is the most aggressive of all brain tumors. He had a partial resection and some chemotherapy, but the tumor did not regress. He came to Dr. Burzynski, and you see the follow-up here is 1995. This is how the tumor looked initially. It's a small tumor but it's a very aggressive tumor. These tumors grow and grow. You see it up here, bright. This is after contrast enhancement. Now two months later you see how this tumor is responding. It's getting faint and certainly smaller. Six months after

treatment it has a little irregular enhancement. Finally, three years later, there is no enhancement, just multiple little dots of holes that are created because tumor has shrunk away.

Ladies and gentlemen, I hope I have made a visual convincing case for Dr. Burzynski's work. Thank you.

Dr. Moss: Whoooo! That's my comment. We're next going to hear from two leaders of the Burzynski patient organization, one of whom is a recovered cancer patient who has taken the treatment. That's Mary Jo Siegel and Steve Siegel. I think it will be more dramatic if I just let them tell their story.

Ms. Siegel: Hi. Seven years ago I was stricken with a fatal cancer, non-Hodgkin's lymphoma, for which no conventional cure yet exists. This disease is treatable for periods of time with chemotherapy and radiation, but the outcome is always death. My husband Steve and I were devastated by this prognosis, but determined to find a cure. Our research took us to the top lymphoma specialists at esteemed medical institutions like UCLA, USC, and the Dana Farber Cancer Institute in Boston, also Stanford. All the experts confirmed our worst fear, that with existing therapy my disease was incurable.

At the Dana Farber Institute a ray of hope emerged with the recommendation that I undergo an autologous bone marrow transplant. This highly controversial procedure would require that I receive extremely high dose chemotherapy and as much radiation as people who were within one mile of ground zero at Hiroshima. I would lose my hair, experience severe nausea and vomiting, and the threat of bacterial and viral infections would keep me in complete isolation for six weeks. My quality of life post-treatment would be drastically diminished. From

the chemotherapy I would become sterile. There would be damage to my heart, lungs, liver, kidneys and bladder. Collateral radiation damage would affect my eyes, salivary glands and thyroid, with a greater than 50% chance that I would develop leukemia if I were lucky enough to survive. I was frightened and suspicious because only a handful of patients had survived this procedure with good long-term results. One such person was the late Sen. Paul Tsongas, who eventually died of complications caused by the procedure. My doctor in Boston said that they would bring me as close to death as possible and then rescue me.

Fortunately, we discovered the work of Dr. Stanislaw Burzynski. He was treating advanced cancer patients with a gentle, non-toxic therapy which he discovered. As I began Dr. Burzynski's treatment, my lymphoma had progressed to a Stage IV. There is no Stage V. Malignant tumors were growing throughout my body. My bone marrow was infiltrated, and there was a large and growing tumor on the side of my neck. After only three weeks on antineoplastons that tumor completely disappeared. Subsequent scans performed at UCLA showed continual reduction in tumor size. I think it's important for people to know that while I was on antineoplaston treatment, I was able to lead a completely normal life. I did the grocery shopping, drove car pools, and attended PTA meetings. I was able to be a regular mother, an absolute necessity when you're raising three teenagers.

More importantly, the drug stopped my supposedly terminal cancer. Within 12 months I was pronounced in remission, not by Dr. Burzynski, but by the same lymphoma expert at UCLA who had told me that I faced certain death. I went off the treatment and remained in remission for two years, when a follow-up scan revealed the possible return of the disease. Immediately I flew to Houston, and Dr. B. prescribed a regimen of antineoplaston capsules. Within five

months, I was once again in remission and have remained cancer free to this day. That's the end of the good news.

Mr. Siegel: I always knew that these results were there, but to hear such esteemed experts as Dr. Schellinger and Dr. Chen say what we always knew, what Mary Jo is living proof of, is so gratifying. The rest of this gets fairly ugly in terms of the politics, which Li-Chuan touched on a little bit. I'll go into a little detail, but I'll be very brief. Remember, the speaker who says he'll be brief is the most dangerous speaker of all.

The tragedy is that our government, namely the FDA, has been keeping what author Tom Elias calls the century's most promising cancer treatment from becoming widely available to cancer patients. This agency has spent untold millions of taxpayer dollars in a systematic attempt to harass, discredit, stonewall, and even imprison Dr. Burzynski. That's why what's going on here today is so important.

As incredible as it sounds, in November 1995 the FDA indicted Dr. Burzynski on 75 criminal counts having to do with alleged technical violations of the Interstate Commerce Act. None had to do with his practice of medicine or the effectiveness of his drugs. Dr. Burzynski had been legally treating patients under Texas state law for some 20 years, the results of which you've seen here today. Not one patient in all that time had ever filed a complaint. If Dr. Burzynski had been convicted on all 75 counts, he could have been sentenced to 290 years in a federal penitentiary. Then you wouldn't have been able to enjoy the results and share with us what we're hearing today.

Are antineoplastons effective? You heard it today. But ask the FDA. It's more poignant. Apparently it believed the answer is yes, because it fought tenaciously to keep the

question of antineoplastons' effectiveness out of Dr. Burzynski's trial. Dr. Burzynski tried to make it a part of the trial. Apparently both FDA and Dr. Burzynski believed he could prove that the drug worked. FDA also fought to keep the truth from the jury by preventing Dr. B.'s patients from testifying, while Dr. Burzynski asked the judge to allow the patients to testify and tell their stories. In the end Dr. Burzynski was acquitted on all counts, approximately one year ago.

We asked Congress shortly thereafter how the FDA could be allowed to squander taxpayer money in an idiotic prosecution the success of which would mean the death of hundreds of cancer patients. FDA was unable to find even a single patient to testify against Dr. Burzynski. Not one. Peter Barton Hutt, a former FDA chief counsel, has said, "If you beat the FDA in court, you have an angry FDA that's willing to slit your throat."

Indeed, while it lost the courtroom battle with Dr. Burzynski, it continues to wage war against him and his patients today. The agency interferes in his practice by telling him who he can and cannot treat. With many types of cancer the FDA requires patients to have failed not one, but two rounds of chemotherapy before they can be treated with antineoplastons. In many cases the chemo has so ravaged their immune system that they literally have nothing left to fight with, and they die.

FDA forbids the use of steroids in the treatment of Dr. Burzynski's lymphoma patients, even when they are needed to temporarily shrink tumors and relieve pain as in Mary Jo's case. Because she was on treatment prior to FDA taking over his practice, Dr. B. was able to inject her with medrol to relieve the pain and the tightness in her neck caused by the tumor.

Now, however, the FDA is not concerned with patient comfort. Rather, their twisted logic dictates that good data collection outweighs human medical treatment and need. The FDA demands that Dr. Burzynski's lymphoma patients stop treatment if they have not achieved 50%

tumor reduction in six months. The absurdity of this typically arbitrary FDA requirement became clear when one Burzynski patient, Frances Langham was forced to go off treatment by the FDA because she had 44% reduction in tumor size. She hadn't achieved 50%. It sounds a little arbitrary to me. She's lucky to be from Arkansas, and politically connected. She received a special dispensation allowing her to continue treatment, but the FDA removed her from the clinical trial. That means that even if she is cured in the future, FDA will count her as a treatment failure in determining how effective antineoplastons are.

These treatment restrictions are applied only to Dr. Burzynski's clinical trials. Lymphoma patients involved in IDEC Pharmaceuticals C2B8 and Elan Pharmaceuticals phenylacetate trials do not have to meet these same treatment criteria. Is it possible that FDA has a bias against Dr. Burzynski, and his patients have to suffer as a result? Who gave the FDA the right to play God? Was it the intent of Congress to give FDA the kind of power it exercises over life and death decisions with no accountability? By denying terminally ill cancer patients access to antineoplastons, this agency literally decides who shall live and who shall die. We have had to watch his children and adults suffer and die as a result of FDA intransigence.

Patients plead to be allowed into antineoplaston clinical trials. Mary Jo and I receive calls every day pleading for our help. The FDA says "No. You don't qualify." Now I ask you, shouldn't it be the doctor, in concert with the patient, making these important medical treatment decisions, rather than an FDA official in Washington who doesn't even know the case? Clearly the FDA is denying these patients their freedom of medical choice, because conventional, FDA approved remedies have failed to work for the majority of Dr. Burzynski's patients. As he told you, he gets the cast-offs from the finest institutions in the United States, if not in the world. Their only choice is antineoplastons or death.

It's been 27 years since President Nixon declared the war on cancer. Public expenditures now exceed 30 billion dollars and private research and development funds must total at least ten times that amount, yet the death rate continues its relentless climb. It's time for a new approach to treating cancer. The only way this will become a reality is by allowing cancer patients expanded access to new experimental and innovative treatments, like we see here in antineoplastons and in Dr. Burzynski's treatment. Common sense tells you this. Until we have an absolute cure, all of it, conventional and alternative, is experimental.

Dr. Nicholas Patronas, Chief of Neuroradiology at NCI, testified under oath that antineoplastons are the most effective treatment for brain tumors he has ever seen. Top oncologists from across the country and around the world, including people you've heard here today and are yet to hear, have lauded Dr. Burzynski's work. Doctors and scientists around the world eagerly await the approval of antineoplastons. In fact, Dr. Michael Friedman, the current commissioner of the FDA, once wrote in an internal FDA memo, "Antineoplastons deserve a closer look. The human brain tumor responses are real." Why is the FDA so determined to impede the progress of a drug with such promising results?

In closing, it's up to this body and this group assembled here today, this group of esteemed professionals, all practitioners, all the coalitions of alternative and complementary medicine, and the consumers, the patients, and the would be patients, to put pressure on Congress to keep the pressure on the FDA to move forward with the approval process for antineoplastons. All the science has been done. Reams of data are being collected from 74 ongoing FDA-approved clinical trials, a little bit of which you got a taste of today. The results are being tabulated, analyzed, and readied for final submission to FDA. In my layman's estimation, the results are nothing short of miraculous. Soon Dr. B. will be ready to file for a

new drug approval, the NDA. But can we really expect the same people who tried to put him in prison for the rest of his life to now turn around and approve the drug that he discovered?

If this attempt fails, and antineoplastons are not allowed into the medical mainstream as a result of a stubborn FDA, then all alternative approaches to medicine are in jeopardy of being quashed by the FDA. All of you need to understand this. Dr. Burzynski really is the spearhead, because the research has been done, the money has been spent, the results are there. If this discovery goes down, it all goes down. We won't have a prayer. Next on the table is the vitamin bill, to regulate vitamins, make them pharmaceuticals. It's coming back again. I understand it's coming up for a vote this year, so it's going to happen. We need your vigilance. We need your help. For any information you need about the patient group, our site is www.burzynskipatientgroup.org. Thank you.

Dr. Moss: We're running woefully behind in terms of the time. We have three commentators. I'm going to ask you all to make your comments extremely brief. Even though we're so far behind, I do want to offer the microphone to anybody who would like to speak on behalf of the FDA. This is a conference about reconciliation, about integration, and I mean that seriously. You know there are two sides to every story. If anybody is in the room from the FDA, not to put anybody on the spot, but I do want to offer the forum to that person if they wish to speak. Yes sir. You can come to the microphone, Dr. Temple.

Dr. Temple: I'm Bob Temple. I'm from FDA, and I'm on a panel later. I can't address most of those things because I didn't get prepared to address most of them. There are a couple

of things people ought to know. First of all, to my best knowledge the indictment was brought by the State of Texas, not by FDA, which can't bring its own indictments.

Panelist: It was brought by the U.S. Justice Department.

Dr. Temple: Okay. There are no data before us now. Don't get the impression that there's a pending application to market this drug. There isn't. If it's being assembled, that's fine. But there isn't anything before us. The people who would review the data have nothing to do with the people who brought the indictment. You may be skeptical about that, but I can tell you that even while indictments were going forward we decided, based on animal and other data, that there was enough interesting about the antineoplastons to let clinical trials proceed. There was actually some discomfort about that, but we thought the two issues were quite separate. Whether Dr. Burzynski was doing the right thing in Texas was a separate question to whether the drug had activity. I'm confident that we are completely prepared to review what data we see. Again, I can imagine some skepticism on your part, but I know that to be true.

We're skeptical about all the treatments we see. It's our job to make sure that they meet appropriate standards. Certain kinds of observations, if well backed up by appropriate documentation – disappearance of brain tumors that haven't had other therapy that might make them do that – are the kinds of observations that have been used to approve cancer therapies in the past. There's an impression that is put around that the only thing we ever look at is randomized blinded trials. That's not true. It's certainly not true in cancer, where certain kinds of responses speak for themselves. You don't have to have a placebo group to know that a tumor that was growing wildly wouldn't have disappeared spontaneously.

All the treatments for testicular cancer, a very nasty, aggressive cancer, when metastatic, have been developed on the basis of what you could call uncontrolled, but in any case are single arm studies. In these, people with metastatic disease who surely would have died within the year were seen to have complete responses that were durable. That was true for the first treatment, cis-platinum. It was true for the next treatment containing etoposide. It was true for the last treatment containing a drug called ifosfamide, where a very small number of responses in the face of what would have been certain death were sufficient to make the case. So if the cases on close inspection look like some of the things that have been described there, I have no doubt that we can review that fairly.

Dr. Moss: No, no questions. I'm sorry. We're not having any. No, sir. I'm sorry. I am sorry, but I am in charge of this meeting. Please sit down, sir. We will have questions, but you are out of order. Actually there's a whole session on that this afternoon.

Thank you so much, Dr. Temple. I think that's really outstanding that you came forward. I should point out that Dr. Temple is participating in this meeting and also is a member of the Advisory Council for the Office of Alternative Medicine. I'm sorry to short shrift anybody.

Arnold Eggers, associate professor of neurology at the SUNY Health Science Center at Brooklyn will make some brief comments.

Dr. Eggers: I'll be very brief. I'm a neurologist, and glioblastoma has been my interest, so I'm very familiar with what's involved here. The usual prognosis of glioblastoma, as many of you know, the average survival is one year. There's about 20% survival at two years. The exact cure rate is not clear, but it's probably in the range of 1 to 2%. The small series published on

these patients shows that unfortunately they all end up demented and spastic as a long term effect of the radiotherapy. That's the outlook.

With Dr. Burzynski's patients, to really know what the cure rate is, first of all there's the issue of initial response rate versus ultimate cure. If chemotherapy is given to patients with glioblastoma early on (BCNU was the first drug), between a third and a half of patients will show objective tumor shrinkage. Unfortunately what happens is this selects out for the faster growing, more malignant, clones of tumor cells. The tumor comes back, and the patients die on schedule. This is seen in many other types of solid tumors as well. Despite an initial response, survival is not prolonged.

I think it's clear here with Dr. Burzynski's treatment that these treatments are holding. They're holding two years, three years, five years. It looks that for patients with this treatment who go into a complete remission for more than, I'm not sure, two or three months, this is going to turn out to be a cure. We know what the numerator is. We don't know what the denominator is, what his cure rate is. I don't know. My guess is something like 15 to 25%. But this is outstanding. This is a breakthrough in treatment of glioblastoma.

I was going to make some more comments. I'm skeptical of his ideas about the mechanism of action, because the ras oncogene is not implicated in glioblastoma, and p53 is seldom involved either. I think some other oncogenes are involved. Thank you.

Dr. Moss. Thank you so much. Dr. Robert Burdick, Clinical Instructor at the University of Washington School of Medicine.

Dr. Burdick: I'm a medical oncologist in private practice in Seattle. I was asked to review some 17 charts that Dr. Burzynski had selected out as having responded to antineoplastons. I was very skeptical when I reviewed these, because I thought all this was garbage. That also should tell you that I'm a mainstream oncologist. These were brain tumor cases. What I found was just as Dr. Burzynski reported, that about 15% of the patients had a complete response, another 20% had partial responses, roughly another 35% had stable disease, and 35% were failures. Dr. Schellinger astutely showed that on his slides.

I don't think there's any question in my mind or his mind that the response that we saw here was due to the antineoplastons. Dr. Temple asked a very pertinent question. Whenever we're doing research of this kind, it's very important to know whether or not the response that you're seeing is due to the antineoplastons or whether it's due to preceding chemotherapy or radiation therapy. There are some people that will respond to those two modalities. But I carefully checked through all of these charts, and in none of these patients was either chemotherapy or radiation given within two months of starting the antineoplastons.

In fact, one of the patients Dr. Schellinger presented had a complete response some two years after the antineoplastons were started. I questioned whether or not she might have had debulking surgery. This patient was in Australia, and I called her physician. I said, "When did this patient have her neurosurgery?" His response was, "What neurosurgery?" The patient's tumor had actually disappeared on an MRI some two years after the antineoplastons were started. This was not the result of surgery, but was temporally related to the institution of antineoplastons.

I followed three patients who have been getting antineoplastons in Seattle in the last year. None of these patients have responded to their antineoplastons. I think that antineoplastons have

a future in the treatment of brain tumors, but there are many questions to be worked out. For example, how long is it necessary to treat a patient before you get a response or determine a failure, since some of these patients had a complete response some two years after antineoplastons were started?

There's a great problem here with expense. Patients tell me it costs them roughly \$6,000 a month for their treatment. Most insurance companies won't cover that. How can patients, even if this is approved treatment, afford this kind of expense? How can insurance companies afford this kind of expense?

The other question that comes up is how toxic are antineoplastons? The 17 patients that I reviewed did not have any life-threatening toxicity, but in the three patients I followed in Seattle this last year, the fatigue, fevers, and weakness were really profound. I do not see much difference in the side effects in these three patients from antineoplastons as compared with receiving conventional radiation therapy or chemotherapy. So in my mind another question is how can we diminish the toxicity of this treatment, so that it can be something that's acceptable and helpful to patients without diminishing their quality of life?

Dr. Moss. Thank you so much. Finally, Robert Newman, Professor of Medicine and Pharmacology and Chief, Section of Clinical Pharmacology, Department of Clinical Investigations, University of Texas, M. D. Anderson Cancer Center.

Dr. Newman: I'm not from FDA, but I am from Texas. I'm not sure where that puts me in the realm of the guilty. I come here today as an advocate not so much for patients, although I clearly am that, but an advocate for drugs. I come from the point of view of a pharmacologist,

trying to understand how individual agents work, what their promise is and what their pitfalls are. Occasionally, when we think we understand how a drug might work, we get naive and perhaps egotistical and think that we can improve the activity of that compound.

Some of the problems with antineoplastons have clearly been the fact that it is not a single drug. We are looking at a mixture of antineoplastons. That has been difficult for us in the scientific community to follow in terms of which compound is being used at a given time, at which dose, for which specific kind of disease. We typically look at those things as well as tumor response. I'm not here today to argue with these tumor responses you've seen. Clearly some of them have been dramatic.

In terms of the doses used, typically we would tend to think about these doses in terms of industrial doses. We're giving grams of this material today. Usually that implies to me as a pharmacologist a nonspecificity to the product. Again, I'm not arguing the fact that there appear to be very dramatic antitumor responses.

I came today to take a look at data. Dr. Burzynski shared some cartoons, if you will, on mechanism of action or proposed mechanism of action for inhibition of farnesyl transferase activity as well as DNA methylation. In point of fact there was no data presented. I can't comment on that. If he does have a specific mechanism involved, and if it does involve ras, and farnesyl transferase, I applaud him. I look forward to the data in a peer reviewed publication that we all can take a look at, with appropriate controls, such as phenylacetate and some of the other compounds that are used in antineoplastons.

Finally, as a pharmacologist and one who is involved in investigational drugs in Phase I trials, I look forward to independent confirmation of activity, independent of the Burzynski clinic, so all of us can take a look at the promise and the pitfalls of this kind of therapy. I agree

with the comment of my colleague that we have not looked at the other side of the coin in terms of toxicity. Just as we've seen Dr. Burzynski on TV in Houston and elsewhere, we've seen some of his patients who have had substantial toxicity. Indeed, we've had them complain about that.

Again, the responses that you've seen are tremendous. We need to take a look at a full disclosure of the promise of this activity as well as the toxicity, so that we can get a full evaluation of it. We have worked with agents which when we first looked at them did not appear to have any activity at all. This involved specific kinds of retinoic acid, derivatives such as transretinoic acid. In point of fact we had to find the right disease for the drug. When used with a specific kind of leukemia called APL, these tumors have a dramatic response. Let me suggest that with further research, in the clinic and in the laboratory, maybe these antineoplastons will find the right kind of tumor for treatment. It is clear that we have very little to offer patients with brain tumors. If these responses are correct and real and reproducible, again, hopefully, outside of Dr. Burzynski's clinic, that's a very exciting finding.

Dr. Moss: Thank you so much. Jim, do we have a few minutes for questions? We have three minutes for questions. There's a microphone over here and people can line up at the microphone.

Participant: Hi. My name is Rita Starr. I'm from the Burzynski Patient Group. What I'm wondering, M. D. Anderson or any of these other big cancer hospitals or centers, it would be nice if somebody provided the money to do independent studies to see if they find also that antineoplastons work. Dr. Burzynski can't afford to do it.

Dr. Moss: Is there a question, Rita? We want to limit ourselves as much as possible to questions.

Participant: You're at M. D. Anderson, right? It would be nice if somebody would provide the funds to do this if it's possible.

Dr. Newman: I agree. M. D. Anderson is a state university. We operate off of state funds. If you can convince the State of Texas to do it, we'll do the trial.

Dr. Moss: Next.

Participant: My apologies for creating a scene earlier, but I do have a bit of a vested interest. To you sir, from the FDA, my understanding in many cases is that before I can participate in any kind of a study, very often I have to be butchered and sutured, have my brain fried with radiation, then be poisoned by chemotherapy. Then I'm eligible for studies. That is true, I understand, in many cases. My question to you is sir, why can I not make this decision in solo or in duality with my doctor, and not have this restriction? (Applause.) I asked the question because I knew almost everyone in this room would want the answer to that.

Dr. Temple: Each of the many protocols that Dr. Burzynski has is initially proposed by him. Then we may or may not ask for modifications of it. For example, if there appear to be established therapies ...

Participant: Sir, that is not answering the question. The question is why do not I have the individual liberty, dealing with my doctor ...

Dr. Temple: Do you want to let me finish? Let me finish. There's a whole session on freedom of choice that's going to discuss all of these questions coming up later. You might want to save some of that for that. In any case, he has written a protocol that he thinks will allow the drug to show what it can do. Where there's an existing therapy that's considered active we may well say that people should have failed that therapy first, because it's an established therapy. But that's the protocol that's written. There can be more than one protocol for a disease. There are some diseases where there's little point in using established therapy, because there isn't anything that works. In those cases there isn't any requirement in the protocol to use a different therapy. It's certainly an issue that needs to be talked about. As I said, it will be in a session that starts at 4:30.

Participant: I'm asking you to talk about it, the individual right ...

Dr. Moss: We have an hour-and-a-half session coming up on exactly that question. I don't think it's necessary. I think you've gotten an answer.

Participant. He's answering it like a politician, that's all. He's not answering it.

Dr. Temple: No, I'll answer it straightforwardly. My belief is that where there is established therapy, especially where it's very effective and curative, people ought to try that therapy before they try an experimental one. There have been some struggles about that.

Dr. Moss: This is the big issue that's going to be talked about for an hour-and-a-half, right in this space, in a few minutes. Next question, please.

Participant: Dr. Burzynski, what data do you have on the effectiveness of antineoplaston therapy on breast cancer?

Dr. Burzynski: In breast cancer we are not doing as well as in brain tumors. This could be understandable because less than 20% of the patients who have breast cancer have abnormality of the p53 gene. We have some stabilizations of the disease. About 50% of the patients involved in clinical trials have stabilization of the disease, but we don't have yet complete and partial responses. We hope that we may see this in the near future.

Participant: I'm a conventional medical oncologist with an open mind. I have a three-part question. Where are you obtaining your antineoplastons? Are you choosing empirically certain antineoplastons in certain diseases? Do you have a program for indigent patients? I see many patients who would not have that kind of money.

Dr. Burzynski: Antineoplastons are produced in a private plant which belongs to our clinic. The plant has been inspected and approved for this purpose by the Food and Drug

Administration. They are made through chemical synthesis and then of course standard pharmaceutical process. What was the next question again?

Participant: Is the choice of which antineoplaston to use for which disease empirical at this point or do you have data on it?

Dr. Burzynski: In our clinical trials we are using four formulations of antineoplastons. In different indications we are using different protocols, but basically these are four formulations which we are testing. We have some other antineoplastons which passed through Phase I clinical trials, but we don't have enough resources and manpower to do Phase II clinical trials. With 74 clinical trials altogether we are extremely busy. But we'll be adding some other antineoplastons. Also we are doing research on a new generation of antineoplastons which in laboratory tests have thousand times higher activity than the compounds we just explained. Hopefully this is only just the beginning and we can have much more effective preparations, and also those which have markedly less side effects.

The side effects which Dr. Newman mentioned and Dr. Burdick stated are usually associated with the large volume of intravenous fluid which patients need to receive. So "water toxicity" seems to be more impressive in this respect than antineoplaston toxicity itself. When you have thousand times more powerful formulations, you don't need to use such volume of water at all, because we can use even transdermal patch to administer them instead of infusion pump.

Regarding the cost of treatment, fortunately more and more insurance companies are paying now for treatment. Every week we see better results in this respect. At this moment it

looks like approximately 50% of the insurance plans are covering the treatment. In the State of Maryland last month, I think a law has been passed which requires insurance companies to pay for patients who participate in Phase II clinical trials in cancer. From the beginning of the year 1999 such law may be extended to all states.

Mr. Siegel: It's our understanding talking with insurance experts around the country that once this drug is approved (hence the need for, the pressure to approve this drug), then it becomes a moot point. Insurance companies will then pay for it much more readily. But until it's approved, you guys hold the key. You guys are the gatekeeper. That's why the ire over this whole issue.

Participant: I would like to ask Dr. Chen and Dr. Burzynski if you might comment. I have heard of patients who cannot afford the treatment but who, because of having known the old oriental practices, have been doing a clean catch urine in the morning and drinking a teaspoon in a glass of orange juice. I'd like to ask Dr. Chen if this practice is still accepted in the Orient. It is not culturally accepted here. Are there any studies about the drinking of one's own urine?

Dr. Chen. Well there's no clinical evidence. It's all anecdotal evidence. It's practiced in Japan, Taiwan and Hong Kong. I have close relatives who did that. Beyond that I cannot tell you much. There are people in the United States who do urine therapy. But I'd like to say urine therapy is not just drinking your own urine. It requires a lifestyle change. If you go and read

those popular publications, they have lots of rules, including not eating fatty meat and alcohol, etc., in the evening.

Dr. Burzynski: Urine is an extremely complex mixture. It contains millions of different chemicals, and we are using only some of them. In the urine you can also find antiangiogenesis factors which are so recently popular. In order to isolate antineoplastons, it is necessary for us to process about 30 gallons of urine for a single patient. It's unlikely that if you drink urine you will find such an amount of antineoplastons. Currently, for the last 18 years, we are producing antineoplastons synthetically, because it's much easier to do it and we are getting much better products.

Dr. Moss. I thank you all for coming and being such a wonderful audience and thank all the panelists and participants, and Dr. Temple. Please move out of the room as quickly as possible. Thank you.