



Treating Lung Cancer: Past, Present, & Future
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GRACE, the Global Resource for Advancing Cancer Education, is pleased to provide the following presentation on Treating Lung Cancer: Past, Present, & Future, by Dr. Ramiswamy Govindan, Director of Thoracic Medical Oncology at the Alvin J. Siteman Cancer Center of Washington University in St. Louis. Dr. Govindan spoke at the GRACE Non-Small Cell Lung Cancer Patient Education Forum in Seattle in September of 2009, a program supported by OSI Pharmaceuticals and Swedish Cancer Institute.

Good afternoon. It's wonderful to see all of you. So actually I have two goals today. I just want to talk a little bit about the practical aspects of treating somebody with what we call locally advanced lung cancer. And then second I just want to give you a flavor of how we come up with a treatment. In general, how do we come up with a treatment that your doctor recommends? And how do we make advances in medicine? I just want to give you a flavor of that.

And as I look around the room, many of us the lung cancer experts here have been doing this for about 15, 10-15-20 years and I have to say we are much more optimistic about the treatment of lung cancer today than ever before. So that definitely should give you some encouragement. We still have a long way to go, but I think in the next 10-15 years the progress is going to be much faster and even today our patients are doing a lot better than what our patients in the past did.

So before we begin, I just want to give a brief overview of how we came to this point. And you have to remember that the chemotherapy history has not been very long. Before 1940s, we never did chemotherapy, and in fact the whole business of chemotherapy began accidentally after World War II when they found that the nitrogen mustard gas ended up dropping blood counts and then they used it in patients with blood cancers and then from there it slowly evolved.

And and these are three gentlemen, one of them, these are the guys who actually began the business of chemotherapy, and in fact this is a 1947 picture of Life Magazine describing a patient getting this ancient drug and which we were using it until even now used sometimes.

And from then, we've really actually moved on to some more sophisticated drugs. And more recently we have a number of drugs. Until 15 years ago, we really didn't have very many drugs for lung cancer. We used one or two drugs.

But now we have a number of these drugs as you can see. I'm sure those of you patients in the audience, some of you may have gotten combinations of these drugs. And I just want to say a few things.

First and foremost, cancer therapy is very complex. And the side effects from all the drugs we give are quite immense, and the management of the side effects is actually quite complex, and I think the best way to approach this is to have a very good communication with your doctor, and nurses. They communicate with you. They help you manage many of the side effects.

One area where we have made significant improvement is the management of side effects. We are much better today in managing the side effects of chemotherapy, particularly nausea and vomiting and all the other side effects

The second thing is, clinical trials are very important. You know this is how we make progress. It's important not for us; it's important for the patients themselves. And there are patients who are still around and doing very well, when some of them participated in some of the earlier trials that even began the business of chemotherapy and radiation. In fact, the very second patient we treated with one of the very early chemotherapy/ radiation trials back in 1990 is still with us and doing really well. So clinical trials provide the best opportunity for patients to get the most optimal treatment, and these things are carefully vetted, and people are actually studying them, and you get some of the best treatment.

The third important point is that we doctors are not very good in telling you how you would do. But we are very good in telling how groups of patients would do. So if you go to the emergency room and doctor in the emergency room tells you you've got this many months to live, this many years to live, I wouldn't take that seriously. We are very good in saying how a group of patients do, but not specifically in how you do.

And I'll give you an example. Several years ago I took care of a patient who actually had a Stage IV lung cancer -- actually I'm still taking care of him. And I give him the usual information that I'm sure your doctors must have given you. And six, seven years later, he's still alive doing very well. So these things are very different; each person is very different. I think it's important to keep in mind.

Some basic principles, I think you should definitely be familiar with the names of the drugs. You should be familiar with the side effects. So you need to know when to not worry about some side effects. And there are some you should be very attuned to, like if you have fever for example during chemotherapy, what you do

Another important fact that's sometimes overlooked is that if you're getting chemotherapy, you may get some nausea, you may get some of these common side effects. And you need to have the medicines to take care of those side effects and *uh* you don't want to be waiting until you have side effects. So it's very important to be proactive about this.

And a couple of issues that come up always — one is what about diet? Does sugar feed cancer? It's a very common myth. And I think it is not true, sugars don't feed cancer. I tell my patients that whatever diet is good for you or was good for you five

years ago, ten years ago, is good for you or whatever is good for your spouse is good for you now. There are no special diets that are known to help cancer patients. And the excessive amount, if you drink ten glasses of carrot juice, it's not going to help you. Sometimes it can even harm you.

The same with supplements. It's a common myth that natural things are good for you. Not necessarily so! And you'll be shocked to know that many of our chemotherapy drugs come from plants and natural sources. When we come up with a chemotherapy medicine, we have identified the active components in the herbs and purify them. We know exactly how much to give; we know what happens. So it's very important to keep those things in mind. And it's very natural to be swayed by some very prominent advertising things on the internet or Uncle Joe tells you that I took this; now I'm alive after 15 years.

Remember cancer is notoriously a diverse disease. What we mean by that is, even if ten people have lung cancer, the same type, treated by the same doctor, same chemotherapy, they'll probably behave in five different ways. And that's because of the biology of the cancer. Cancer is a disease of the genes. We have about 30,000 genes in each and every cell of our body. And a typical cancer like lung cancer, at least about 50-100 genes get messed up in different ways. And depending on what set of genes get damaged and how much they are damaged and, how far they are damaged, people do differently even if they have the same stage and same extent of tumor. And they behave very differently, and in fact we are beginning to unearth all those things, and we will do so better in the coming years.

It's never too late to stop smoking. It's possible that they actually influence the outcome, and there are a couple of good where patients actually did better. One important thing is when you smoke, you develop bronchitis more often that can lead to pneumonia. So when you stop smoking those things don't happen, you don't cough, so that's a very immediate and tangible benefit. So, certainly those things are good things to do.

More specifically with chemotherapy and radiation, it's very hard to predict how things will go since we give chemotherapy and radiation simultaneously, it's important to keep in mind certain things. The first two weeks you'll wonder what all the fuss is about; things will go fine. You may just have fatigue and nausea. As things go along, third, fourth week you begin to have difficulty in swallowing, and that in some patients gets to a point that we may have to even put a stomach tube, feed them for awhile and give intravenous fluids; even though it sounds a little bit awkward and bad, it's actually okay. Patients get through that and once we finish everything, they tend to heal up pretty well and they maintain their nutrition.

The key, and the one important principle in this, especially with stage III treatment with chemotherapy and radiation, is to keep the nutrition going with either normal intake or a stomach tube and keep the fluid intake appropriately enough so that they don't get dehydrated. And so once we finish all the treatment, it takes a few months before you heal up completely. It's going to take a few months before you feel

like normal again. And it's very important to know what you're getting into; not to scare you, but it is important to know that chemotherapy and radiation is not an easy thing to take. And when you go through this, there are going to be some real lows and there are going to be days you'll feel fairly normal. But it's important to appreciate the fact that after a few months as long as the cancer is under control, people almost always recover, recover to a near full extent and able to carry on with normal activities.

So in the next some years I think we're going to make progress by using better chemotherapy drugs. We already have three of them being tested. Our radiation technique is improving rapidly, and what seemed like the Stone Age if you look at the radiation planning ten years ago -- we are becoming very, very good.

Finally, I think we'll make progress only through custom-tailored therapy. What is customized therapy? So there are two goals of our customized therapy. One is to tell you that this drug can be very toxic for you. And the second is to tell you this drug will be very good and effective in your tumor. So there are two pieces. You know when you get a drug, either the drug can be very effective on the tumor cell; and the drug can be very toxic. So both may not necessarily go hand in hand. And there, of course, patients who have the double whammy effect where the tumor doesn't get killed and you have a lot of side effects.

So in the coming years we will separate the two. If possible, we'll identify who should not get a particular drug, or who should get a decreased dose of a particular drug. Every drug is a poison and can seriously hurt patients because we all wired differently. And that's the field what is called pharmacogenomics.

So here is an example. The idea is to take a group of patients and take a group of patients who are going to have severe side effects and remove them and identify patients who are not going to respond and then suddenly we are focusing our effect on one particular group of patients. Can we do that? Yes we can.

And one example is, this is an example of a drug that some patients would get for colon cancer. You give it, a significant number of them will have severe toxicities, like diarrhea and low blood counts. Why? Because this drug, as it gets metabolized, it becomes less active and doesn't produce toxicities. This is an enzyme that turns an active drug into an inactive drug and this particular enzyme doesn't always function at 100% capacity. You may have 30% capacity of this enzyme. I may have 100% capacity of this enzyme. If this function is working at a low capacity, guess what? This more active drug lingers around a lot longer. You may say -- why, that can be good! Not necessarily -- that can cause a lot of side effects. And now we have means to test this, a single blood test, a simple blood test and we can know the results within a couple of days and based on that, if we have this particular genetic makeup you have, we tend to give this drug at a lower dose or we don't give this drug at all.

That's one example of how we can spare patients from severe toxicities. And more importantly, how can we select patients for better therapy? I told you that each tumor is

quite different. And I also told you that the tumors have multiple genes have gone wrong, not just one of two genes. Now we have techniques where we can actually look at thousands of genes at one time, and we have new techniques that actually scan the tumor for several thousand genes and these are, this is one example.

This is how the test would look under a sophisticated computer that actually can scan them. If you look at this, these are green and red dots, and this is one kind of a pattern. This is a different kind of a pattern. Based on that we can actually tell with 90% accuracy those who will do very well and those who will not do well. And three or four groups are now rapidly developing tests that we can use on patients; not yet ready for prime time, but we are getting there very closely.

The second way we talked about is that the chemotherapy causes DNA damage, and we have about 80 enzymes or so to repair the DNA damage. And that's why you don't get skin cancer when you lay down on a beach. So what happens in cancer therapy is that when you give chemotherapy that damages the DNA, and if you're very good in repairing it, what happens is the cancer cells survives. And the key is to identify patients who will have very good DNA repair capacity, and a wide range of drugs that work this way. You can kill cancer cells in different ways. One is to damage the DNA. So the implication is if you have very good DNA repair capacity, you don't want to use this class of agents, but you can use different kinds of drugs. So that's an example of how we can select patients for treatment.

And finally, these are ways we can make advances. And cancer is a very complex disease. We are not going to make progress overnight. This is an example of a real picture of how this cancer cell thrives by multiple different pathways. If you block this pathway, the cancer cells will find a way to survive by using this alternate thing. It's like imagining that if you put a road block here on this street you can block all of traffic in Seattle. We used to be very depressed looking at these kinds of pictures, but now we know that even though this happens, the cancer cells preferentially use this one path. This is the concept of addiction, and cancer cell gene addiction, so now we know if we can identify the tumor that will depend on this pathway, we can develop drugs that will knock this off. If tumors are addicted to this pathway, we can knock things off through this pathway.

One thing we are doing now is that you remember the human genome project, which actually sequenced the entire genome of the patient, and now we are doing sequencing and tell cancer genomes to find out what are the genes that are mutated that we don't know about, how we can come up with new treatment. This is a small machine about the size of your dishwasher that actually scans the tumors and sequences the entire genome of the cancer cells, and that's being done in a few places, including our place, and by that we will find out new pathways, new drugs, and that's how we come up with a new drugs.

And finally, smoking is important, and in the future we'll not be doing the CT screening on every patient. We'll be finding our tumors or patients who are likely to get lung

cancer, and then we'll screen only those patients. Already now three groups have found out some genes that actually put you at high risk of developing addiction to cigarette smoking and also put you at high risk of developing cancer and very soon, in about 5-10 years we'll have tests that we can identify patients with high risk for cancer developments and screen those patients; not everybody and anybody. So I think the field is quite promising and I think we are moving forward in the right direction. So be hopeful.

Thank you.