Breakthrough Lung Cancer Treatment Approved
Webcast
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Renato Martins, M.D., M.P.H.

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Introduction

Andrew Schorr:
Just at the end of August [2011], the Food and Drug Administration (FDA) has given fast track approval to a new drug, crizotinib, or trade name Xalkori, in the fight against lung cancer. You'll hear from a lead investigator from the Seattle Cancer Care Alliance, next on Patient Power.

Hello, and welcome to Patient Power, sponsored by the Seattle Cancer Care Alliance. Thank you for joining us for this breaking news interview about groundbreaking progress in the fight against lung cancer, specifically non-small cell lung cancer, a subtype of that actually. Non-small cell lung cancer accounts for about 187,000 new cases in the US every year of the overall 220,000 cases of lung cancer. And the breakthrough is the fast track approval of a new drug, crizotinib, or Xalkori is the trade name, and this helps a small percentage, but significant, of people with non-small cell lung cancer.

To help us understand this is Dr. Renato Martins. Dr. Martins has been a lead investigator in studying crizotinib, and he is the medical director for thoracic, head and neck medical oncology at the Seattle Cancer Care Alliance. He's also an associate professor at the University of Washington School of Medicine. Dr. Martins, what is the name of the new drug, and what makes it significant?

What is Crizotinib?

Dr. Martins:
Well, the name of the new drug is crizotinib, and what makes it significant is the fact that for patients that have advanced lung cancer and a specific mutation in the tumor cells — so this is not something one is born with, this is a mutation that occurs in the tumor cells only — but when that mutation is present their chance of benefitting from this drug is extremely high, three times higher than it would be from benefitting from conventional chemotherapy.

Andrew Schorr:
So this is where I think people in the trials were taking two pills a day, and then you saw just a remarkable shrinkage of the tumors?
Dr. Martins:
That's correct.

Andrew Schorr:
Had you ever seen anything like that before?

Dr. Martins:
Well, these responses are — I guess the best comparison would be the responses to erlotinib when an EGFR mutation is present. We certainly see comparable responses.

Andrew Schorr:
Let's go back just a few years. So before 2004, I understand people with non-small cell lung cancer — and that's the vast majority of people diagnosed with lung cancer, maybe 187,000 or 85 percent of the 220,000 Americans who are diagnosed with lung cancer every year — I understand that it was treated pretty uniformly before, and then things began to change. And this is yet a new part of that change.

Dr. Martins:
That's correct. So in 2004 we became aware that the presence of an EGFR mutation increased the chance of a response to a specific pill or a group of pills that we have, and we now know years later that it's actually better to give such a pill instead of conventional chemotherapy. The patients have a much better quality of life and a much higher chance of response than with conventional chemotherapy.

Andrew Schorr:
All right. With crizotinib now, this new drug, also known as Xalkori is the trade name, so now we have another example where if someone is diagnosed with that gene mutation you have a, if you will, personalized therapy for them?

Dr. Martins:
That is correct. So, you know, in the past we gave chemotherapy to everybody, and some benefitted, others did not, and we didn't know why. And now we can deliver a much better tolerated therapy, and we know up front that they have a very high chance of response based on the specific genetic traits.

Andrew Schorr:
So we should make clear, though, either with the EGFR mutation or the ALK mutation, though, and the pills someone can take where we have remarkable shrinkage of their tumors, in neither case is it a cure, right?

Dr. Martins:
We do have a few patients that have gone years receiving erlotinib if they have EGFR mutation. You know, crizotinib hasn't been around for that long, so we don't have anyone that's been taking it for five years or longer. You know, with that said, it is likely that this — these drugs are going to afford a temporary disease
control and not a cure. That has become pretty clear with the use of erlotinib in patients with the EGFR mutation.

And although we have much better therapies to offer to them these days, we must continue to work hard in improving their therapy even further, expanding the time that the disease is under control or perhaps one day being able to just make it go away altogether.

**Andrew Schorr:**
As far as an advance in lung cancer, though, and I know this is a smaller percentage of people with non-small cell lung cancer, it's still a big deal, isn't it?

**Dr. Martins:**
It's a very big deal, and as we move into identifying subgroups of patients we are going to be able to deliver therapies that are tailored to their specific tumor, which obviously will decrease toxicities and increase in efficacy.

**Andrew Schorr:**
Dr. Martins, I know the FDA, besides approving this new drug approved a test. So that's part of the paradigm, isn't it, is that you're testing patients to try to better understand their version of lung cancer, if you will, and then have the appropriate therapy?

**Dr. Martins:**
That's correct. The FDA approved the test that actually identifies the presence of this genetic alteration in the tumor cells.

### What to Expect When After a Lung Cancer Diagnosis

**Andrew Schorr:**
So when someone is diagnosed with lung cancer today, and I know trials continue to go on, what should they expect? They should expect a work-up, if you will, of what is their specific situation and then see whether in new approved therapies like this or even ones in research, is there something that is specific for that?

**Dr. Martins:**
Yeah. I would say that most guidelines that have been recently published, and that's certainly our approach here at the Seattle Cancer Care Alliance and the University of Washington, is that if you have a non-small cell lung cancer and you do not have a squamous cell carcinoma, then we would test for the presence of EGFR and ALK, A-L-K mutation, which is the mutation associated with the response to crizotinib.

The chance of having this mutation is directly related with someone's smoking history. You know, if someone has a less than 10 pack/year of smoking, which is a pack a day for 10 years, the chance of having this — one of these two mutations may be as high as approaching 50 percent. If someone is a heavy smoker, then
the chance of one of these two mutations is much smaller, you know, perhaps somewhere between 5 and 10 percent, but it's such a dramatic change in their therapeutic options that we test everybody that has a nonsquamous cell carcinoma.

**Andrew Schorr:**
Now, I know it comes up, and sometimes it's very surprising to people, there are those who are diagnosed with lung cancer who never smoked.

**Dr. Martins:**
Mm-hmm.

**Andrew Schorr:**
Would they have a higher likelihood if they never smoked and developed non-small cell lung cancer to have one of these mutations like ALK?

**Dr. Martins:**
Yes, absolutely. Just like I explained, that chance for having one of these two mutations for a nonsmoker may approach 50 percent.

**Clinical Trials and Ongoing Research**

**Andrew Schorr:**
Now, we mentioned that you have been an investigator of this new drug, and of course you're very devoted to clinical trials. You have other clinical trials going on in lung cancer to try to make more discoveries?

**Dr. Martins:**
Oh, we have many clinical trials open. We are exploring issues of stimulating someone's immune system to fight the cancer. We are exploring what one would call second-generation pills that would target EGFR mutation. Just as a couple of examples.

**Andrew Schorr:**
So are you encouraged? Here we are with yet a second gene mutation and a drug that's now developed and will be on the market for it. Are you encouraged? You've been at this a long time.

**Dr. Martins:**
Absolutely. And, you know, as I explained to a patient today in the clinic, pretty soon we're going to be looking back at this time and wondering how poorly we treated patients. We are doing so much better now, and that future is not too far ahead.

**Andrew Schorr:**
Dr. Martins, now, this drug, crizotinib, was really approved fast. It got, if you will, fast track approval. Am I right?
Dr. Martins: Yeah, and that is a scenario that happens when something has such dramatic results that it doesn't necessarily require a randomized phase 3 trial to prove its efficacy.

Andrew Schorr: So this was based on a phase 2?

Dr. Martins: Yep. And end results of a phase 1 as well.

Andrew Schorr: Wow. Now, we were talking a moment ago about trials you have going on. Are there three specific trials you wanted to comment in lung cancer at the SCCA?

Dr. Martins: Well, as I said before, we have trials investigating the role of someone's immune system in fighting the cancer. We have trials with investigating the role of what one would call, you know, second-generation inhibitors of the epidermal growth factor pathway, you know, among others.

Andrew Schorr: You said you were encouraged. So for someone who is in this journey, this fight in lung cancer, and if one approach isn't working, is there the hope, whether in a trial or maybe now with a newer medicine that there might be something that would work?

Dr. Martins: Absolutely. And I think that the option of exploring clinical trials is one that should always be considered. Remember, you know, this drug was in a clinical trial before it was approved, and that is obviously important to keep in mind.

Andrew Schorr: Right. And I bet you and so many of us owe a debt of thanks to the patients who participated.

Dr. Martins: Absolutely.

Andrew Schorr: Now, one last thing, what is the expectation then of a patient who currently is benefitting from this new drug? We really don't know how long it will be effective or for whom. Is that correct?

Dr. Martins: Well, we know for whom. We don't know what is the tail of the curve, what is the percentage of patients that can go, you know, a year, two years, three years or perhaps longer taking this pill.
Andrew Schorr: Okay.

Dr. Martins: The drug hasn't been around for that long for us to have a good idea of what that number might be.

Andrew Schorr: So the bottom line is we have yet another drug, an example of personalized medicine in what has been a daunting cancer, lung cancer, and another sign of progress in what just a few years ago was a really tough fight.

Dr. Martins: Yep. That is correct.

Andrew Schorr: Good news for the fast track approval of crizotinib, or Xalkori, for people with this subtype of non-small cell lung cancer, and also as we heard encouraging news as research goes on to personalize treatment in lung cancer and with the hope of a cure.

Thank you to Dr. Renato Martins, medical director for thoracic, head and neck medical oncology at the Seattle Cancer Care Alliance, associate professor at the University of Washington School of Medicine, and maybe most importantly in this case a lead investigator for crizotinib.

Dr. Martins: Thank you.

Andrew Schorr: I'm Andrew Schorr. Thanks also to the Seattle Cancer Care Alliance for sponsoring this breaking news program. Remember, knowledge can be the best medicine of all.

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