



**Case-Based Expert Roundtable Discussion
Drs. Janessa Laskin & Alan Sandler
Asian Never-Smoker with Adenocarcinoma: EGFR Mutations and Tissue Testing**

Howard (Jack) West, MD
January, 2010

Dr. West: Hi, I'm Jack West, medical oncologist at Swedish Cancer Institute in Seattle, Washington. I'm also the President and CEO of GRACE, the Global Resource for Advancing Cancer Education. And I'm happy to be here today at a Thought Leader Round Table with a couple of my friends and colleagues in the lung cancer world. They are Dr. Janessa Laskin, who is a medical oncologist at the British Columbia Cancer Agency in Vancouver, BC, Canada, and also Dr. Alan Sandler, who is the Chief of the Hematology/Oncology Division at the Oregon Health Sciences University in Portland, Oregon. So, thanks very much for coming.

Dr. Sandler: Hey Jack.

Dr. West: We're just going to talk about some interesting controversial cases. The field of lung cancer is evolving quickly and there are a lot of situations that don't have a right answer, and they're going to be individual differences in practice patterns. So I thought we'd talk about some real life scenarios and hear what you actually do.

So the first one is a 53-year old Asian never-smoking woman who actually presented by being at Pike Place market and feeling short of breath when she was going up some stairs, and that was new for her. She saw her physician, ended up getting a chest x-ray that showed an infiltrate in the right lower lobe and also some additional nodules. She had a biopsy that showed an adenocarcinoma with BAC features. And the question is, she comes in for a first visit with evidence of metastatic disease right now. The PET scan confirms that several of her other lesions are also PET avid and this is a diffuse process throughout the lungs.

So we have just seen some publications that came up in the New England Journal of Medicine in the last couple of months that suggest that there could be a real value in testing for EGFR mutations upfront. Is this something that has impacted your practice? If you had a patient come in who's a never-smoking Asian woman, how are you going to approach this patient? Are you going to start them on chemo or an EGFR inhibitor automatically or are you going to do testing?

Dr. Laskin: Of course, this is a really common scenario, since about 50% of my patient population is Asian are a lot of never smokers. So this is really my bread and butter; I see this everyday.

I think that the role with EGFR mutations is evolving. I think we have to remember that it doesn't answer the question of everyone who responds to an EGFR inhibitor. But it certainly does identify a very, a select group of people who really have a much greater chance of a fantastic response to these agents, and the trial that you're referring to with gefitinib, or Iressa, versus chemotherapy in the first-line setting really did show impressive results if you knew someone was mutation positive. So I think if I know someone is mutation positive, then I would be tempted to offer an EGFR inhibitor in the first-line setting. If I don't know that someone is mutation positive, then I still think they do better off with chemotherapy until you do know what their status is. So it hasn't yet affected my practice, or the practice in Canada, because we don't have access to the EGFR mutation testing yet as standard of care. We are actually developing that, and there's a national program now that's identified five labs. I'm actually proud to say that Vancouver is one of the five labs that has been identified to standardize how we're going to test for EGFR mutations in anticipation that will become an issue for first-line treatment and we'll be able to test people with a rapid turnaround time, and then potentially offer them the drug.

Dr. Laskin: So I guess it's a longwinded way of saying it hasn't impacted my practice yet, but I think it will. In reality, I think if you're EGFR mutation positive, as long as you get one of these drugs at some point in your course of treatment you benefit. I'm not sure it really matters when you get as long as you don't miss the opportunity to get it.

Dr. West: Alan, what do you think?

Dr. Sandler: So I think that's a very good point the last point that Janessa made is that although the data is preliminary in the IPASS study,

it appears as if the survival for the two groups was similar, even in the mutation positive. So I think there are two key points for the IPASS: We no longer really should assume that the clinical profiling of a patient is as good as the genetic testing. And so because it clearly looked as if chemo was actually better at least initially in the wild type. So I think that if we're thinking about first-line EGFR TK therapy, you have to test for the mutation. And if you don't have the tissue, you should attempt to get it if the patient is willing.

Dr. West: I think it is an impressive corollary of the IPASS trial that 60% of the Asian never-smokers with an adenocarcinoma have this. But 40% did not and they were not well served by the first-line TKI.

Dr. Sandler: Right.

Dr. West: So Alan, you alluded to this. If she didn't have tissue available, are you speaking to patients now about getting a biopsy for this or for anything down the line?

Dr. Sandler: So now having moved from Nashville, Tennessee to Portland, I saw three patients yesterday that were never-smokers with lung cancer which I think in Tennessee that could have been a year's worth of folks.

And actually one that I saw yesterday, a 43-year old Asian female, she actually was born and raised in Hong Kong who has metastatic disease and the initial biopsy was actually brushings from a bronch, so there was no tissue. So we had a long talk about what to do. She unfortunately also had small but significant brain metastasis with edema, and so she needed to have radiation therapy. So that's a three-week plus period of which she really wasn't going to get any other therapy anyway other than the radiation.

So, we offered her the opportunity to have another biopsy and we'll have the time for testing.

Dr. West: What kind of turnaround are you experiencing or expecting today because that's one of the practical issues. If you have somebody who's been diagnosed with metastatic cancer, the thought of waiting a week or two is different from waiting three or four or more weeks?

Dr. Sandler: That's right. And I'll defer, I don't know if Janessa has experience with sending it out or know about it yourself. But we, I haven't done it.

Dr. Laskin: Our goal when we're developing the program in Canada is to, if we're thinking about this in the first-line setting, is we need a less than 3-week turnaround. In reality, and perhaps this is a Canadian bias, in reality biologically speaking, I don't think waiting three weeks to start your first-line chemotherapy for metastatic disease is a huge issue. Psychologically, it's absolutely a barrier for people, and I understand that. But we actually have 2-week wait lists to start chemotherapy anyway. So I think for patients asking them to wait 2 ½ weeks to get this result is reasonable, if it's going to have a huge impact on their treatment. But that's what we're targeting. I don't know if that's going to be a reality yet. I do think it's going to have to be inside of a couple of weeks to be a practical test.

Dr. Laskin: I think one thing that we may need to consider as tissue is becoming more and more of a hot topic and very important in the management of lung cancer is trying to perhaps involve our pathology colleagues more closely

and earlier on because if the pathologist had the ability to decide if a given test should be done like an EGFR mutation, then that would cut down the wait time. Of course that would mean that the pathologist needed to have a lot of clinical information. So I'm not sure how that will work.

Dr. Sandler: Well, that's actually a good point as to who should be tested to just test the never-smokers, to test all the adenos and hope that you hit a few that were smokers that are actually mutation positives because that's probably the most exciting find there-- that you have somebody who had a 30-pack year smoking history and they're an adenocarcinoma and you decide to test and -- oh my gosh, they've got the mutation. That sort of makes everybody feel pretty good.

Dr. West: Sure, and there are plenty of people who don't have an enormous smoking history: the mutation rate is not negligible in ex-smokers, especially with a limited number of pack-years and who quit a decade or two ago.

Dr. Laskin: So this is one the issues we're trying to deal with as we think in Canada about who we're going to test, and it's come up that we should perhaps test adenos. But the problem with that is that a lot of these biopsies are extremely small. And its very hard for pathologists to be definitive about whether its an adeno or not. And I know from experience, because we finished a first-line trial of Tarceva® in selected patients in British Columbia. Out of 65 patients, we had 22 EGFR mutations and ten of those were in "not otherwise specified". So we would have missed 40% of the EGFR mutations in that population if we'd only tested adenos.

Dr. Laskin: Well I think those people probably did have adeno -- its just that the biopsy wasn't sufficient for the pathologist to call it adeno.