Interview with Dr. Janessa Laskin on Adjuvant Chemotherapy for Early Stage NSCLC by Dr. Howard (Jack) West January, 2009

Dr. West: Hi, I’m Jack West, medical oncologist at the Swedish Cancer Institute and also the President and CEO of GRACE, Global Resource for Advancing Cancer Education. I’m here today, with Dr. Janet Laskin, who is an assistant professor at the University of British Columbia in Medical Oncology and has a particular interest and expertise in lung cancer. She is also on the faculty for GRACE and I’m very happy to have her involved. So, thank you very much, Janessa.

Dr. Laskin: Thank you, Jack.

Dr. West: In the postoperative setting for patients with earlier stage resected non-small cell lung cancer, which are the patient settings in which you’re definitely included to recommend chemotherapy and which are the patient groups in which you’re going to individualize it and consider it much more of a gray zone for patients.

Dr. Laskin: Obviously, when you’re thinking about adjuvant chemotherapy, you have to always consider the individual patient and how fit they are and how well they’ve made a postoperative recovery and whether or not they’re going to be able to tolerate the chemotherapy because, as you know, the chemo that we use in an adjuvant setting is moderately toxic; and so people have to be relatively fit in order to tolerate it and get the benefit out of it. But that being said, I think that there is fairly convincing evidence that chemotherapy in the setting of Stage IIIA disease when that is resected, obviously Stage II disease and I think those are the two clear cut settings for adjuvant chemotherapy for the people who have Stage IA disease, so the quite small tumors. I think Stage IA cancers, although they definitely have a risk of cancer coming back, I don’t think our chemotherapy is good enough yet to provide a reasonable benefit for chemotherapy in that setting.

Getting to the gray zone I think is IB disease, so tumors that are a little bit bigger but without any nodal involvement. There has been some evidence to suggest that in patients who have high-risk Stage IB disease, chemotherapy might be useful. Although, that’s never been studied in a very clear-cut way, when you look at meta-analyses which is a bunch of data put together, I think that if you can try and separate what high risk is, then you may identify a patient group that will benefit. I guess that is officially a gray zone for me because trying to define what high risk is, is a little bit tricky.
What I tend to use is tumor size so anything over 4 centimeters I do look at tumor grade. So something that is very poorly differentiated or looks really nasty under the microscope, I may be more inclined to offer adjuvant chemotherapy in that setting. I do actually consider age, although, I think that in general age is a no-no when you’re thinking about therapy in lung cancer. I would be more tempted to treat a younger person with Stage IB disease than I would to treat someone say over 70.

Dr. West: Would your approach be any different for never-smokers? I’ve seen some patients who have at least discussed and some have actually received recommendations to receive EGFR inhibitors or some such approach.

Dr. Laskin: I think that’s interesting. Because I practice in Canada the available of drugs in an office-label setting like that is quite limited. So patients would have really wanted it and they would have to pay for it. In our medical system, we’re not really used to paying for chemotherapy drugs or paying for anything for that matter. I think that I would like to see a study that actually really defined never-smokers with EGFR inhibitors in an adjuvant setting. I think that’s possibly a good route to go. I’ve never recommended it personally. I think it’s intriguing. But I don’t think there’s any evidence for it at the moment.

Dr. West: Now, there have been some preliminary studies. Some tests like ERCC-1 are still preliminary but have emerged as possibly contributing to the ability to refine better who is going to benefit more or less with postoperative chemotherapy, at least cisplatin-based chemotherapy. Are you sending for this or other molecular markers when you consider treatment for patients after surgery, or how interested would you be in even discussing this if it was available?

Dr. Laskin: I think is where things are going in lung cancer and cancer in general is trying to identify these kind of molecular markers or biomarkers, as we call them, to try to figure out who we should be treating and who we shouldn’t, because obviously all non-small cell lung cancer is not the same and we shouldn’t be treating it the same. And obviously only some people benefit from chemotherapy and we shouldn’t be inflicting it on everyone only to benefit a few if we can possibly help it.

I think ERCC-1 is a great example of something that’s very interesting. Not to open another can of worms, but its similar to K-Ras, in I think these two are the furthest advanced in terms of some of the studies that are happening for predictive variables in chemotherapy response. I am testing for it now. What we are trying to do is test for it retrospectively, that is to go back in all of our patients that we have treated over the last
few years and do the ERCC-1 levels and see what has happened to them. I think that would make our institution more comfortable with the ERCC-1 testing because it's not a very simple test; it's actually quite reader-dependent, so you have to make sure that you're an expert at reading it. So I think we need to gain some comfort level with it. And I think internationally we all need to get comfortable with doing this test.

For me, one of the issues is that basing your chemotherapy on ERCC-1 when it hasn’t yet been proven in a prospective randomized trial, it's a little, well its controversial. Because what you're doing is you're potentially withholding a treatment. For example, we know that cisplatin-based therapies are best in an adjuvant setting, and this is a curative setting. When you do an ERCC-1 test, you may potentially get a result that says you should not treat somebody with this state-of-the-art treatment; rather you should give them something else or perhaps nothing at all. I'm a little uncomfortable withholding treatment based on a test that doesn't have more evidence with it, when there aren't really other options to treat people.

Dr. West: Potentially you might a different threshold for somebody in whom it's a consideration, but in the gray zone versus somebody for whom it would otherwise clearly indicated.

Dr. Laskin: Yeah. Or if there was a proven alternative, if, for example, I believed that non-cisplatin-based adjuvant therapy was just as good, and then I could choose between one or the other. But I don’t think we've actually proven that definitively, so I would be concerned at this point, we don’t know enough yet to withhold a standard treatment for someone. However, my guess is that in the next few years we will figure that out.

Dr. West: For adjuvant therapy, what is your current preferred regimen or do you individualize it and use a wide range of treatments for your patients.

Dr. Laskin: No, we use what we consider has the most evidence behind it, and of course it was a Canadian trial that helped usher in the new era of adjuvant therapy, if I can say that, the BR-10 study. And not that regimen was cisplatin and vinorelbine, and although we have altered how we deliver it slightly to reduce the toxicity, which is what I consider standard therapy. Occasionally, if someone really has a strong contraindication to cisplatin-based therapy, I have used carboplatin/taxol, because that was also used in other adjuvant studies. But my strong preference is first cisplatin regimen.

Dr. West: Janessa, thanks for taking the time.

Dr. Laskin: My pleasure. Thanks.