

**Case-Based Expert Roundtable Discussion
Drs. Janessa Laskin & Alan Sandler
Asian Never-Smoker with Adenocarcinoma but no EGFR Mutation: Considerations
for First Line and Maintenance Therapy**

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- 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.
- Dr. West: 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 if this particular person, an Asian never-smoker with an adeno BAC subtype is tested and actually comes back EGFR wild type, how are you inclined to proceed with treatment specifically?
- Dr. Laskin: Assuming that she's well and wants treatment and so on, I would offer her a platinum-based doublet therapy. My standard is usually cisplatin/gemcitabine but I think that a lot of these regimens are fairly interchangeable with EGFR wild type. I think the IPASS data did clearly show that this was better in a first-line setting. I probably would eventually offer her an EGFR TKI, but not in the first-line setting.
- Dr. West: Where has Alimta® fit in the algorithm in Canada as a general practice, as well as your personal view on it in somebody with an adenocarcinoma?
- Dr. Laskin: Well, at the moment we're limited by the availability of Alimta® in the first-line setting. So, I can't get it in a first-line setting and patients would have to pay for it which I don't personally feel that incremental benefit in

adenocarcinoma is worth my patients paying a huge amount of money for it in a first-line setting. They can get it second-line or as potentially as maintenance therapy; we'll have to see how that goes. But there's not a province right now in Canada that offers first-line pemetrexed outside of a clinical trial.

Dr. West: This is a patient who actually does not have any contraindications to Avastin®. She had a brain MRI that looked okay. No history of coughing up blood. Do patients who would be eligible for it get it in Canada? And if not that routinely, is that systematic decision or a personal one for the oncologist in Canada?

Dr. Laskin: So, I think Avastin® is a great drug. I don't think we know yet who exactly it's a great drug for. But I do think that there are certain populations who will greatly benefit from this drug. Although its approved for first-line use in Canada by Health Canada, it's not funded in any of the provinces. So there are some people who would have private insurance that would pay for some of it. But by and large people aren't getting it off of a clinical trial just for financial reasons.

Dr. West: And Alan, obviously you have a history with setting what is arguably a standard of care for standard chemotherapy based first-line treatment. Can you tell us a bit about your thought process?

Dr. Sandler: Yes, I think going down the line in this particular patient, you do the mutation testing to see if any EGFR TK inhibitors are an appropriate first-line. But as you mentioned, these patients are also perfect candidates for bevacizumab as long as they don't have brain metastasis and they're not coughing up blood. And so for wild type that's what we would consider we would do the paclitaxel/ carboplatin, and Avastin® would be the choice. It's true that, you know, Avastin® we've gone the other way, although in the TK inhibitors we've tried to identify the population that responds. Avastin® we've identified populations that we shouldn't give it to for toxicity; not necessarily efficacy.

Dr. West: And how long would you continue you her on that three-drug combination versus stopping and either watch at that point or continue some of the agents?

Dr. Sandler: So the Avastin® story is actually a true maintenance story. We will probably be talking about maintenance therapy, as its been called. But you know maintenance in the truest form is receiving first-line therapy and then continuing some of that down the road. So in this we would do, say 4-6 cycles of chemotherapy with Avastin®, and then when the chemotherapy is done -- and I typically stop at four -- the Avastin® would continue as maintenance every three weeks until progression or toxicity.

Dr. West: And you're not inclined to add anything else in at this point beyond the Avastin® if someone is not progressing after the initial carbo/Taxol®/Avastin®?

Dr. Sandler: I'm not. There are developments that have occurred, and I don't know if we're going to roll into those now, but there are the developments of docetaxel (Taxotere®), Alimta®, and Tarceva® having been used as sort of early second-line therapy, or its been called maintenance as well, showing improvement in progression-free survival, in some cases survival.

Dr. West: Yeah, so let's. If I'd asked the question as a general principle if you have somebody who is not progressing and has a good performance status but has residual disease, has gotten four cycles of in one case a carbo/Taxol® and Avastin®, in another case say you gave carbo and gemcitabine. Are you inclined to watch them off of treatment; continue just one of these agents or switch to something new?

Dr. Sandler: So the one thing that I don't do and wouldn't consider is continuing the same therapy. I don't do more than generally more than four cycles of chemotherapy with a very rare exception. And I don't continue part of the therapy as maintenance other than the Avastin®. The question of early second-line therapy with either Tarceva®, Alimta® or Taxotere® I think is an interesting development. But in my opinion seems to suggest that second-line therapy works and that it's important that we give it to our patients. But I'm not so sure that it has to be done immediately after and I tend to favor the chemotherapy holiday because no matter how well a patient is doing with chemotherapy, I guarantee you they'll feel better without it.

However, what I am more mindful of, I think, is the fact that there maybe some patients who don't have that wonderful initial response or even good stable disease that maybe would be benefited by early second-line therapy and not pausing to see if you, because you might lose them if you wait a couple of months.

Dr. Laskin: Yeah, I agree. I think that's the key issue is not to lose the people who are going to potentially benefit from second-line treatment and I completely agree with Alan on this point, not just because he trained me.

Dr. Sandler: That doesn't hurt.

Dr. Laskin: That doesn't hurt. But because I do think that a chemo holiday when you're talking about people with realistically a limited life span, to have some time off of chemotherapy I think is very valuable for a number of reasons: Not just to let your body recover a bit, but also to give you some time to do

things that you might want to do and being tied to getting chemotherapy every three weeks and risks of infection and so on, at least with the cytotoxic agents, I think is not going to benefit everyone. I do think that there are some select people, maybe 10% of my practice, who maybe would be good candidates for switching to an early second-line agent, but I agree the fundamental part is just not missing that opportunity to give them second-line treatment.

Dr. West: So you both probably see your patients regularly, how often maybe a monthly basis or so?

Dr. Sandler: So I do about every other month with scans. Although I think in patients who maybe don't appear to be as robust, I might just see them monthly, not necessarily do scans ---

Dr. West: Right.

Dr. Sandler: But see them a little more frequently.

Dr. Laskin: I tend to see people after their first-line chemo, I tend to see them at about six weeks just to make sure that they're not progressing quickly. Sometimes with a scan at that point just to see the whole effect of the treatment and then about every two months after that.