



## **Case Based Panel 2019 – Lung Cancer ALK Positive**

### **Case Based Panel Discussion – 2019 ALK Positive, Progression After Success on ALK Inhibitor**

For this round of case based panel discussions, Dr. Jack West is joined by Drs. Jonathan Riess and Suki Padda. Jonathan W. Riess, MD MS is Associate Professor of Medicine in the Division of Hematology/Oncology at UC Davis Comprehensive Cancer Center. Sukhmani Padda MD is Assistant Professor of Medicine (Oncology) at the Stanford University Medical Center.

In this video series, the doctors discuss a series of cases related to a diagnosis of ALK Positive NSCLC. This next panel discussion is regarding progression after success on an ALK inhibitor. Do you continue the ALK inhibitor when transitioning to a chemo based treatment?

- Dr. Jack West: Let's take the case of a patient who has been on, alectinib Alecensa for ALK positive metastatic disease, presented with brain metastases that were without symptoms and over that course of treatment developed three brain metastases that needed to be treated but then did well. Eventually after three years Progress's in the body but not in the brain. How concerned are you that you would need to continue an ALK inhibitor just to cover the risk in the brain in terms of this is somebody who has had initial brain metastases then progressed transiently on alectinib. So my question is basically when you have a patient where you're concerned you're going to need to switch to chemo, do you keep, would you consider concurrence ALK inhibitor just to control the brain as well? Or at some point do you just have to abandon, worrying about intracranial brain control and put it all on the chemotherapy at that point?
- Dr. Jonathan Riess: So in terms of maintaining, you know, maintaining CNS, you know, CNS control, that's really critical in ALK lung cancer. You know, as we talked about before.
- Dr. Jack West: CNS being central nervous system or brain.
- Dr. Jonathan Riess: And First Line alectinib really dry out, you know, the CNS, the central nervous system brain benefit really helps drive that, that progression free survival. You know when they, when they progress on that. I, I mean I think the short answer is it depends. I think the like most things I think, you know, with patients who are going to go on chemo with



carboplatin, pemetrexed it is a very good drug across the blood brain barrier. So I think in situations like that you don't necessarily need to continue the ALK inhibitor.

Dr. Jack West: Can I just interject by asking you, when we use pemetrexed Alimita a lot in lung adenocarcinoma, it's very good drug and maybe preferentially favorable in ALK-positive. Are you talking about using it as a single agent or as a combination?

Dr. Jonathan Reiss: I would in a patient who hasn't had chemotherapy, I would typically use it in a combination with carboplatin and pemetrexed, and then you know, sometimes with bevacizumab as well, there's a suggestion that other younger, Avastin, the younger patients may, especially with these oncogene driven tumors, may be more sensitive. Tumors may be sensitive to this, you know, the [inaudible] admission strangling the blood vessels that feed the cancer. I would just highlight that, you know, the keynote 189 study that looked at carboplatin pemetrexed and pembrolizumab, Keytruda, did not look at ALK patients or NGFR patients. So I generally, with that, if I'm going to do Carbomal pemetrexed, I generally do not add the immunotherapy.

Dr. Jack West: So, Suki, what are your thoughts about, you know, how much do you worry about and factor in risk in the brain at the time that you're thinking about transitioning to a chemo based approach?

Dr. Sukhmani Padda: I factor it in a lot. So I think if a patient has had only body progression without brain progression on Alecensa and they have a history of brain metastases but they're super well controlled, I would be very nervous to abandon Alecensa. It's kind of a similar principle that we're seeing in other types of lung cancer. EGFR mutated for example, where we're thinking about continuing [inaudible] at the time of progression for patients with a history of brain metastases, but are progressing in the body. So I think this question is applicable to a lot of types of lung cancer where we have good oral drugs with brain penetration that control the brain. But with, you know.

Dr. Jack West: It's very frustrating because we don't have combination data to speak of, but the concept, the rationale is very strong. So I think that many of us are inclined to cobble it together or at least think about it seriously, but we need data to speak to.

Dr. Sukhmani Padda: I think that's, that's absolutely true. There's not really published data or presented data. But, the one thing we do have to think about when we're combining a targeted therapy with then chemotherapy is about safety. So we just have to be mindful of that too.

Dr. Jonathan Reiss: I would just highlight that, you know, in patients with ALK lung cancer, who haven't had brain metastases to start. I'm still very vigilant about checking for brain Mets. So, you know, normally at the time of progression, I, you know, typically for my non small cell lung cancer patients get a brain MRI as well with systemic progression to see if it's also



spread to the brain. But aside from that, even if things haven't progressed systemically, if they're on Alecensa, you know, every six months or so, I will get a brain MRI. I don't know if that's your practice as well.

**Dr. Sukhmani Padda:** Yeah, for me it depends a little bit on how good the drug is. Like crossing into the brain. If the patient doesn't have a history of brain metastasis and the drug is very well known, like Alecensa to get into the, I may do annual surveillance. And then of course, anytime you see a body progression you need to check the brain.

**Dr. Jack West:** I agree with that, but, you know, if you have a patient with Outbrain metastasis and have them on an agent that is very good in controlling within the brain, I think that would lower my suspicion. And not to say it never looked, but I don't know that we need to look every few months when the pretest of the probability of finding progression is very low in the absence of new symptoms. Of course, if someone has new brain, you know, headache or vision changes, that would change everything. But, and as would progression in the body raise the probability of something. So it's always worth looking at.