



Case Based Panel 2019 – Lung Cancer ALK Positive Case Based Panel Discussion – 2019 ALK POS with Brain Mets, Radiation before 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.

The doctors discuss a series of cases related to a diagnosis of ALK Positive NSCLC. In this video, the discussion is regarding a patient with ALK positive asymptomatic brain metastases. Is the standard approach of focal radiation before beginning ALK inhibitor appropriate, or do you begin with the ALK Inhibitor?

Dr. Jack West: Let's turn to the case of a patient who is diagnosed with metastatic lung cancer. Has a good performance status, not a lot of other medical problems, has an ALK rearrangement, and has a brain MRI done in their routine staging that shows four small and asymptomatic brain metastases. And this is not that rare. We find that patients with EGFR mutations and especially those with ALK rearrangements will have a pretty common scenario of brain involvement and at some point, whether it's initial or over the course of their illness. How inclined are you to favor having them start on the alectinib or some other ALK inhibitor rather than go to the radiation oncologist to get focal radiation to treat those small lesions? Are you comfortable with that or do you feel that the historical standard of starting with radiation should be the way to start and then proceed with whole body therapy after that's completed? Jonathan?

Dr. Jonathan Riess: I'm completely comfortable in patients with ALK metastatic lung cancer with small asymptomatic brain metastases to start off with alectinib with Alecensa. I think, you know, the trials like the Alex trial allowed patients who had asymptomatic brain metastasis. And I think that the intracranial, you know, the, the concentration that gets in the blood with these drugs is basically comparable, the concentration that gets in the brain, it's got great activity in the brain. That's one of the major reasons that patients derive this progression free survival benefit is it's brain activity. So my practice in those patients is to start out with Alecensa, and not your brain radiation. I also, I often have them go see the radiation oncologist to kind of get established, get their input, kind of getting to know you, but I really disfavor brain radiation in that situation. And in



particularly whole brain radiation therapy, you know, they can get long-term neuro cognitive side effects with whole brain radiation therapy. Now that patients, particularly with these oncogene driven cancers like outlive years and years and years, you know, you wouldn't, you want to do all possible to delay, especially whole brain radiation to try to really avoid those neurocognitive side effects.

Dr. Jack West: Suki, do you have that same level of comfort?

Dr. Sukhmani Padda: Yeah, I think if there are four very small brain metastases without any symptoms, absolutely. I like Dr. Riess, also like to involve my radiation oncologist early, at least for a meet and greet, even if there's going to be no treatment offered at that time, from radiation standpoint, at least my patient has met with the radiation oncologist, knows who they are and knows kind of what they do. So if we ever need to use that in the future, that at least is not a total unknown. Sometimes for patients where it's not so straightforward, you know, where the brain metastases are little bit larger maybe, you know, or symptoms like one, one and a half centimeters. Or if they're in a location where if they grow, it's going to be a really big problem, then sometimes we can even work with our radiation oncologist to treat the higher risk brain metastasis and kind of let Alecensa do the rest in terms of taking care of what may remain.

Dr. Jack West: So I think that that's been a real change, that we have way more confidence in the ability of some of these newer targeted therapies. Many of them directed against ALK, some for EGFR inhibitors, especially in the newer ones like, Tagrisso, Summerton for those with EGFR mutations to expect that they're going to do a good job to treat the disease we see and also suppress the potential for future progression in the brain.

Dr. Sukhmani Padda: Absolutely I think the reason why we feel so confident is because it's a nice, at least, you know, from the most basic chemical structure of the drug that they're looking to see that hopefully this particular drug is going to cross into the brain. And it's also great to see, you know, clinical trials that are allowing eligible patients to come on with untreated brain metastases. So we do feel confident when a drug like this gets approved in terms of how we manage our patients.

Dr. Jack West: It's instructive now that we have tools that can treat brain metastases. We're studying that much more. Jonathan, you raised the point that the issue of brain radiation to particularly whole-brain radiation would even piecemeal spot welding radiation with stereotactic radio surgery. We're much more judicious about this, judicious about this. We didn't use to worry that much about radiation because we didn't have patients living long enough to have this be a complication. And in the patients with driver mutations, we have the good situation of them living for years now being much more prone to us seeing that the [inaudible] of remote brain radiation and our concern about over-treating that if we can reserve that option for only the few cases where that's needed.

