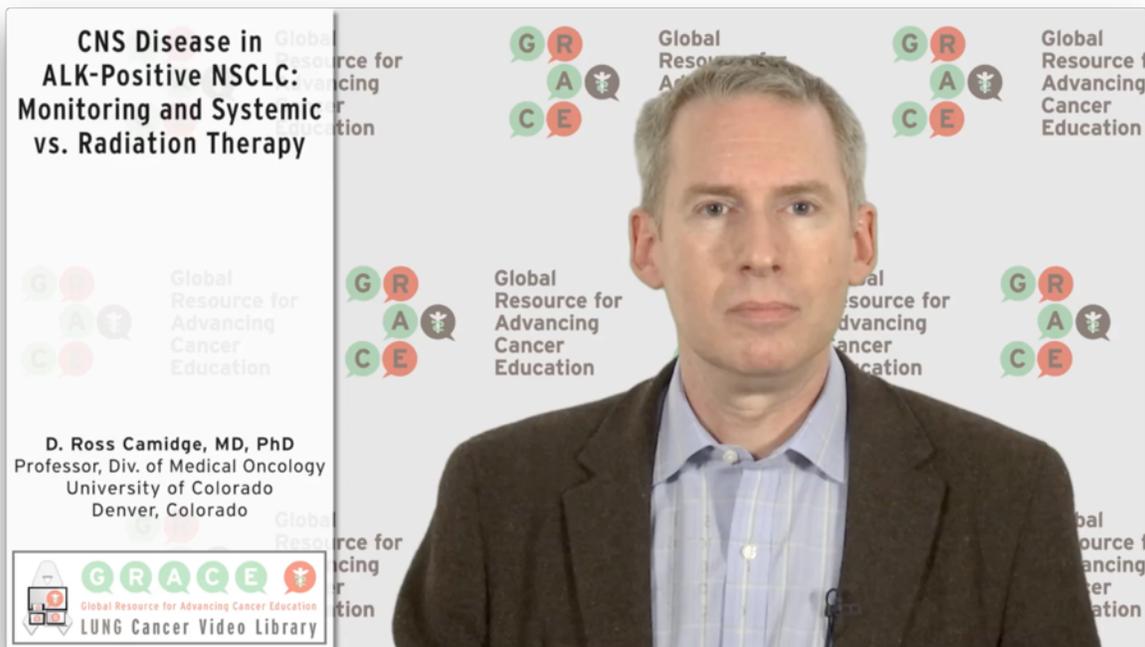




CNS Disease in ALK-Positive NSCLC: Monitoring and Systemic vs. Radiation Therapy



TRANSCRIPT & FIGURES

As we started to treat ALK-positive patients with crizotinib, it became clear that the brain was somewhat of an Achilles heel. It was a common site for people, when their cancer started to grow, for that to be the site where their cancer was growing, and we know that in many of those cases that's the only site where the cancer is growing. We know from a small number of studies where people have actually sampled blood levels and from the fluid around the brain that actually very little of the crizotinib is getting in, so it's maybe just that you have a relatively under-treated part of you.

Now that plus the fact that people fortunately live a long time with ALK-positive lung cancer means that the brain can become this area that will crop up with disease. For me that means you should absolutely keep an eye on the brain. If you have no known disease in the brain I would do an MRI scan at least every six months. If you do have known disease in the brain, even if it's treated, I would be looking more frequently, possibly as frequently as one scanning the body on treatment, or maybe half as often.

Now if you do have disease in the brain, because the activity of crizotinib is not zero, unless you have a lot of symptoms from the disease in your brain, many people will start on the crizotinib, but obviously keeping a close eye because if you do progress in the brain, then you may have to salvage it.

You can salvage it in a number of different ways. One would tend to stay on the crizotinib and either have local radiotherapy or occasionally surgery depending on the site of the deposits in the brain. For me though, there's a difference between one type of radiotherapy and another. For example, you can either treat the whole brain, what's called whole brain radiotherapy, or

you can treat individual lesions with what's called stereotactic radiosurgery or SRS. I very much prefer giving SRS, even to a reasonably large number of lesions, than whole brain radiotherapy for the simple reason that people with ALK-positive disease are now living long enough that they're manifesting the side effects of whole brain radiotherapy and that can mean word finding difficulties, memory difficulties.

So I think for me if you're just at the point where you can spot weld a few areas with stereotactic radiosurgery, that's fine – stay on the crizotinib. But if someone is thinking about whole brain radiotherapy, I would probably switch to a next generation ALK inhibitor rather than do the whole brain radiotherapy because we know they have good activity in the brain.

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