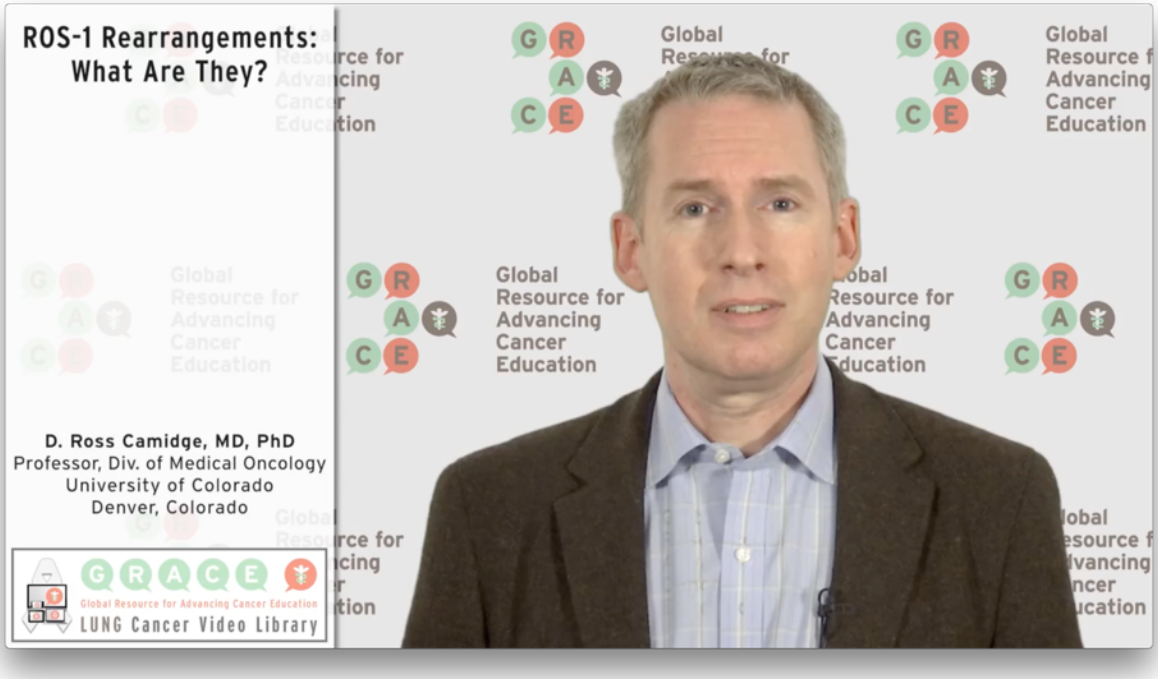
Global Resource for Advancing Cancer Education

LUNG Cancer Video Library

ROS-1 Rearrangements: What Are They?

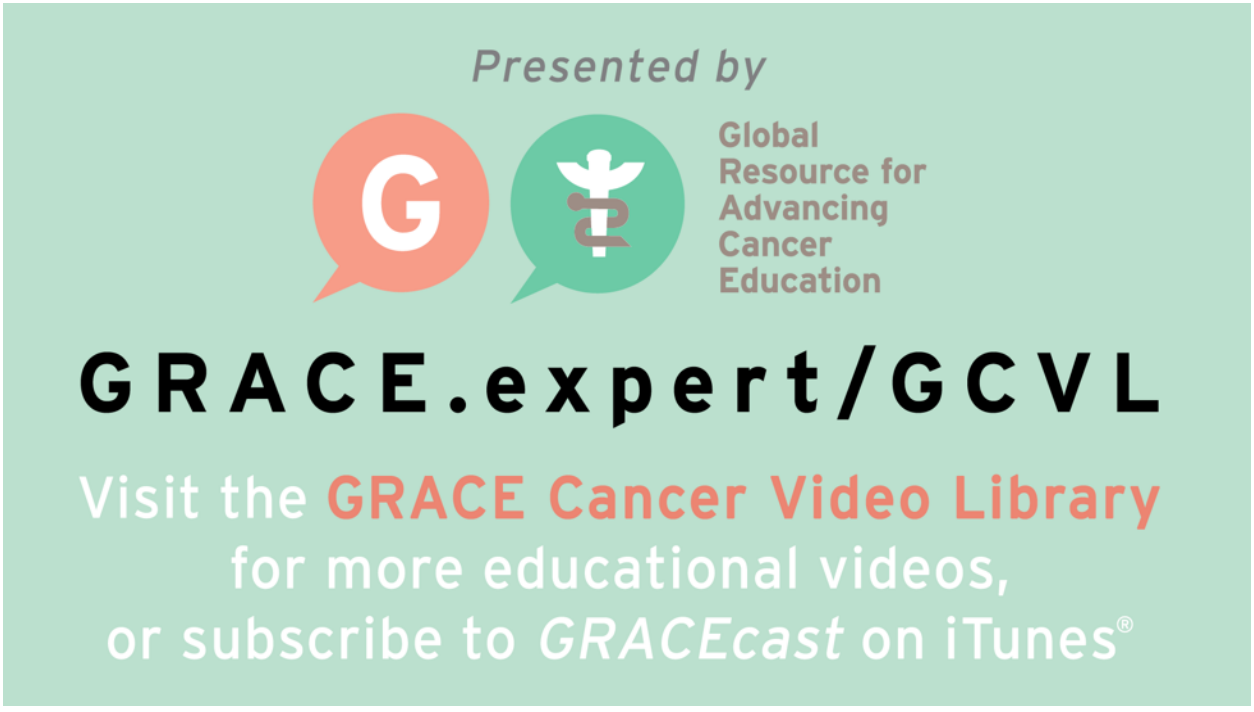


TRANSCRIPT & FIGURES

ROS-1 rearrangements are like the sister to ALK gene rearrangements. They're also a gene which is silenced in most adult tissues, which is turned on again by a gene rearrangement creating what's called a fusion protein which can drive the cancer cell. Structurally they're very similar to ALK rearrangements and they respond to many of the same drugs. Particularly crizotinib, the first licensed ALK inhibitor, has also clearly shown good activity in ROS-1 driven cancers.

They're rarer, maybe one quarter as common as ALK rearrangements or less. There are subtle differences. The benefit of crizotinib in ROS-1 gene rearranged lung cancer actually seems greater than it is in ALK, so the response rate is 70% as opposed to 60%. The median progression-free survival, the time it takes for the cancer to grow, on average is about 19 months as opposed to nine or ten months with ALK.

People are wondering about why the difference is, and there are various theories. Maybe crizotinib is actually a better ROS-1 inhibitor than it is an ALK inhibitor. Maybe the frequency of progression within the brain, which we know is somewhat of an Achilles heel for crizotinib and ALK-positive lung cancer — maybe that's not such an issue with the ROS-1 rearranged patients simply because they have a lower frequency of deposits in the brain. Increasingly on a biological level, we've also seen a little bit of data that ROS-1 may be a more genetically simple cancer that ALK. It occurs in a part of the genome, part of the DNA of the cell, which is more structurally stable, so its ability to mutate and evolve in the presence of the drug and then progress later may be less. Either way, it's a good thing to have if you have it.



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