



2022 Case Based Panel Discussion

Sotorasib vs. Adagrasib as Treatment for KRAS G12C Mutated NSCLC

Speakers:

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TRANSCRIPT

Dr. Dagogo-Jack: And so earlier we said that, you know, a lot of these immunotherapies are interchangeable, right? We're using, like, pembrolizumab, durvalumab, atezolizumab, etc. Do we feel that way about the- the KRAS G12C inhibitors, I guess, Josh or Kathryn? Do we think that they're the same? I know, of course, we always have to pause and say no one did a study where we put them directly against each other. Right?

Dr. Reuss: Yeah, Yeah. So, I mean, I would say overall, simple answer. Yes slash we don't have enough information. You know, I think both target the KRAS G12C. We have had limited efficacy data on both. I don't think there's a clear winner there. I think from a toxicity profile, also not a clear winner. You know, you can look at numbers looking slightly different between studies. I would say the only thing that we have more for Sotorasib than Adagrasib is we do have the phase three data comparing it to Docetaxel chemotherapy, which for the longest time has been our subsequent line therapy in this space where we did see that it improved the progression free survival number.

But unfortunately the study did not have enough people in it to really power it, meaning it didn't have enough statistical validity to look at overall survival. So I think in the immediate term, I think probably one could say they are relatively interchangeable. But I think we do need more information. There's obviously lots of trials ongoing at combining these medicines with other treatments that affect the signaling pathway of the mutation. And so I don't think that the story has been fully told.

Dr. Arbour: I would agree that the official answer is that and I agree with that sentiment is that, you know, what would I use in the second line setting? Probably the fourth option, that either drug is fine,



but if forced to make a choice between the two and if I'm writing a prescription and saying, do I choose Sotorasib or Adagrasib, I would say in a patient with brain metastasis, we don't have great data about the efficacy of Sotorasib in patients with central nervous system tumors that are untreated.

The Adagrasib clinical trial did report data on showing response rates in this setting and so that are fairly similar to the overall response rates of Adagrasib in other areas of the body. And so I might be inclined in a patient knowing that the efficacy is pretty similar of the two drugs. They work mechanistically, very similar. The toxicity is very similar in a patient with brain metastasis. If I'm going to choose between the two, I may be more inclined to choose Adagrasib, which is the drug that was most recently approved but have been really in parallel development this entire time as a part of clinical trials.

We also, as was mentioned by Josh, thinking about can we combine these drugs safely with other drugs in the setting of, you know, clinical trials that are ongoing. It also remains to be seen how safely these drugs can be combined with immunotherapy, if they will be safe after immunotherapy or before immunotherapy, the sequence of therapy may matter, and those will be answers that will be needed to be answered by ongoing clinical trials and clinical research that we're all doing to try to identify the best treatment strategies for a patient, not just with one therapy, but- but looking at the entire natural history and disease course of a patient.