Transcript Details
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Side Effect Management in ALK+ Non-Small Cell Lung Cancer Care

Announcer:
Welcome to *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. Urs Weber, an Assistant Professor in the Division of Medical Oncology at the University of Colorado Anschutz Medical Campus. He'll share insights on managing side effects in ALK-positive non-small cell lung cancer treatment. Here's Dr. Weber now.

Dr. Weber:
With ALK-positive lung cancer, having seen the CROWN data and how much better the long-term outcomes with lorlatinib are than with any of the prior ALK TKIs, I think my goal is to get people on lorlatinib if at all possible, because it's just the most effective drug that we have for this disease at this point. I think there is a lot of wiggle room with the dose of lorlatinib, more so than I think most people appreciate. And so the label dose of lorlatinib is 100 milligrams. But when you look at the CROWN update that was presented at the ASCO Annual Meeting, it actually showed data from patients who had dose reductions to 75 or even 50 milligrams of lorlatinib, and it really didn't compromise the long-term efficacy in any sort of significant way. What it does change is the toxicity. Most of the side effects of lorlatinib, as with many other drugs, are dose-dependent. One of the troublesome side effects with lorlatinib, especially in elderly patients, is the neurocognitive side effects. So that's a broad catch-all term, but it can include anything from brain fog to mental slowing to forgetfulness to mood changes. And for older patients who are maybe already experiencing some cognitive impairment, already experiencing some of those symptoms, that can be a real problem. Those side effects are dose-dependent, so they are more likely to occur at 100 milligrams and less likely to occur at 75 or even 50.

And so for patients who I'm worried about struggling with some of the side effects of lorlatinib because they're elderly, or because maybe they take some medications that interact with lorlatinib, those are the patients where I'm not at all worried about putting that patient on 50 milligrams or 75 milligrams, because it seems like the long-term efficacy is comparable. I think you really want to make sure that you're balancing the efficacy of the treatment with the side effects and making sure that their quality of life is preserved, especially over that long of a timeframe.

If they really cannot tolerate lorlatinib, even at 50 milligrams, it's better to be on an ALK-targeted therapy than to not be on ALK-targeted therapy at all. So I do think those are patients where I would still consider alectinib or brigatinib, the second-generation TKIs, because they do well. They produce multi-year progression-free survival intervals on average. And so when you have an elderly patient, two, three, or four years is a meaningful amount of time. And so if the neurocognitive side effects are an issue, I think there's definitely still a place for the second-generation drugs.

Some of the other ALK side effects, like the edema and things like that, seem to be consistent across the different TKIs. I haven't had very much success switching TKIs and getting that to be any better, but certainly, the neurocognitive side effects seem to be pretty unique to lorlatinib.

Announcer:
That was Dr. Urs Weber discussing side effect management in ALK-positive non-small cell lung cancer. To access this and other episodes in this series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!