Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/guideline-recommendations-for-first-line-treatment-of-advanced-nsclc-with-targeted-therapies/29134/

Released: 11/27/2024
Valid until: 11/27/2025
Time needed to complete: 1h 03m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Guideline recommendations for first-line treatment of advanced NSCLC with targeted therapies

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Yu:
This is CME on ReachMD, and I'm Dr. Helena Yu.

Dr. Gubens:
And I'm Dr. Matt Gubens.

Dr. Yu:
Dr. Gubens, in patients with metastatic non-small cell lung cancer and select actionable mutations, targeted therapy has really become the standard first-line treatment. Matt, what are the guideline recommendations for patients with common EGFR mutations or ALK fusions?

Dr. Gubens:
Of course for EGFR, osimertinib has long been the standard of care. Median overall survival 18 months, excellent tolerability. But this year we have 2 new options added to the guidelines along with osimertinib. One is from FLAURA2. The opportunity to give osimertinib plus chemotherapy, which showed progression-free survival, though not yet overall survival, benefit over osimertinib alone.

And the other trial, which provided amivantamab, the bispecific antibody against EGFR and MET, as well as lazertinib, a third-generation TKI, again, with progression-free survival, but not yet overall survival, benefit over osimertinib alone.

This really enriches the conversation. It's a longer conversation with patients because these are really viable treatments. We really have to think about patient-specific factors. Do they have higher-risk disease like significant brain metastases, multiple co-mutations, especially TP53, or even thinking about exon 19 vs L858R. We also have to think about sequencing, because the one thing about EGFR is if I don't give amivantamab in the first line, I can always give it second line. If I don't give chemo up front, I can give it a second or third line.

And ALK, of course, we've also had a TKI option for some years. We started with crizotinib and then we had the second-generation agents, alectinib and brigatinib, and now we have lorlatinib as well. Any of the second- and third-generation agents are appropriate preferred first-line options, but it's important to note data that emerged this last year at ASCO 2024, the CROWN data, which was lorlatinib versus crizotinib, has shown us that the median progression-free survival in that population has not even been reached at a 5-year point. So I think a lot of us who have all along given lorlatinib in the second line at the point of resistance on alectinib and brigatinib are actively kind of thinking about using it first line.

Helena, what can you tell us about guideline recommendations for patients with some of the other actionable mutations?

Dr. Yu:
Yeah, it's hard to go through them all, so we'll focus on a few. These are all rare driver mutations. So ROS1. Right now there are, in the NCCN Guidelines, 3 preferred ROS1 inhibitors. The first one is crizotinib. That was our original ROS1 inhibitor, a drug that we're well familiar with that we've used in the ALK and MET exon 14 space historically.

Then along came entrectinib and repotrectinib. Both much more ROS1-specific, but also having NTRK inhibition as well. And I think that comes into play in regard to side effects. I think entrectinib and repotrectinib, both great medications that have slightly enhanced efficacy over crizotinib and, in particular, greater CNS penetration, so really good intracranial disease control. But the flip side of that, of course, is some of the neurotoxicity. So sometimes they can be a little bit difficult to manage with our patients. And again, dose reductions can be helpful in that space. But really have equipoise between the 2 newer agents.

So for RET fusions, we actually have 2 options, pralsetinib and selpercatinib. Both great RET inhibitors with excellent, again, both intracranial and extracranial activity with median progression-free survival north of around 14 to 16 months. I think RET inhibitors also have unique toxicities. You can get diarrhea, hypertension, dry mouth, some elevation of liver function tests as well, but generally very well tolerated. And then finally, MET exon 14 skipping mutations, there are 2, again, preferred MET inhibitors in the NCCN Guidelines, both capmatinib and tepotinib. Both have better efficacy in the, I think, frontline TKI treatment-naïve space and so would prefer to use these as first-line treatment. And then with MET inhibitors we do see unique toxicities as well with lower extremity edema and hypoalbuminemia being something that can be quite impactful for our patients.

Matt, you discussed our options for common EGFR mutations, so what is your practice now if a patient comes in with a common EGFR mutation? Do you have a standard treatment that you utilize, or are there sort of different populations you give different options to?

Dr. Gubens:
Again, I have a conversation with everybody, I want to share the data we have. I will say that for a lot of patients, I'm still using osimertinib first line. Maybe with the exception of patients with just exceptional burden of disease. Even brain mets don't faze me because we really can control them with osimertinib alone or with directed stereotactic radiosurgery.

What about you?

Dr. Yu:
Same. I think that without the overall survival data, which I admit might compel me to change my practice, I really have been giving osimertinib as my default and then, maybe after shared decision-making for select patients, choosing to escalate here. But I do really like having multiple options in the later-line setting as well.

Well, that's all the time we have today. Thank you for a great discussion, Matt, and thanks to our audience for listening.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/Prova. Thank you for listening.