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https://reachmd.com/programs/cme/the-long-game-mastering-treatment-sequencing-across-the-disease-continuum/36293/

Released: 07/31/2025
Valid until: 07/31/2026
Time needed to complete: 1h 06m

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The Long Game – Mastering Treatment Sequencing Across the Disease Continuum

Announcer:
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Dr. Cho:
This is CME on ReachMD, and I'm Dr. Cho. Here with me today is Dr. Leighl and Dr. Kerr.

Dr. Leighl, now let's review a patient case of someone who has been treated with osimertinib first line. What can you tell us about this patient?

Dr. Leighl:
Thanks. So this was a recent case of mine, a lady who's very well educated and an informed patient advocate. She was diagnosed with an EGFR exon 19 deletion-mutant lung cancer. She had involvement of bone and lung, and she was on osimertinib.

I remember our conversation at 18 months. I bring my patients in, if they're doing well, approximately every 3 months; we'll do imaging and a clinical assessment. And at 18 months, she was very anxious. She said, “Oh, I need my scan. I need to come in and see you. I'm very stressed.” And we went through everything, and she was fine, and she continued to have a very nice response to osimertinib. And she told me that part of her anxiety was because this was the median in FLAURA where patients started to have progression. At month 21, she called and she said, “Something’s wrong. I think I have a pneumonia or something. Can I come in?” So we brought her in, and sure enough, she had a significant cough—dry cough, more short breath. She didn’t look right. We did an X-ray—very high-tech in Canada, and she had clear progression of disease on X-ray. We were able to accelerate her CT scans, which showed marked lung progression.

So we had to make some decisions. We were able to get her an urgent bronchoscopy and very quick sample. And then in discussion with her, we agreed that we were going to start systemic therapy and then tune our plan based on the pathologic and molecular results later on over time. But we just really didn’t think we could wait. Radiotherapy alone wasn’t going to be a good enough option just based on the progression of disease and the extent.

So she said to me at that point, she said, “I know that platinum has been the standard. I know with MARIPOSA-2, we really want amivantamab and chemotherapy.” And so in Canada, we had a program where we could access that.

And we were very fortunate. We were able to get it all together very, very quickly and start her on amivantamab and chemotherapy.

And one of the things that I love about this regimen is that it’s both targeted and untargeted. You don’t require biomarkers to go on this, but it clearly adds more than just chemotherapy. It also adds on-target EGFR and also MET. So really covering a broad range of resistance mechanisms.

So she had symptom improvement. Fortunately, pathology review showed adenocarcinoma. The NGS, interestingly, over time came

back, and we still found her EGFR exon 19 deletion. And the only other thing that we found was a mutation in beta-catenin, but nothing else, CTNNB1.

So we didn't need to change therapy—amivantamab plus chemotherapy was already working. And so even if I had found something else, you could argue would I have changed management? And I probably wouldn't have, given that she's clinically benefiting.

Now we're out several months. She's actually had a very nice partial response on the COCOON regimen. So of course, much, much easier for her in terms of the patient burden.

So, Dr. Kerr, always so challenging to get that molecular diagnosis. Any comments from you about this case or things you folks are doing?

Dr. Kerr:
Yeah, thanks, Dr. Leighl. I think your case does raise a number of issues that we often do wrestle with, the most important of which is our ability to obtain a tissue biopsy at disease relapse. As you pointed out, this patient being an example, things were progressing really quickly, and depending on the access you have to a diagnostic modality, it may be really difficult to actually get that sample and get it processed in time, raising all the questions that we've already covered around turnaround times in the laboratory.

And again, for individual treatment decisions but also for informing practice more in general, if it's at all possible to get some material, to get information about possible resistance mechanisms, then it's a good idea to actually try and get that.

Dr. Cho:
So I think I really agree on your approach here, Dr. Leighl. We sometimes see our patient's condition deteriorate too rapidly to get tumor tissue or even get plasma NGS results on time.

So I think without biomarker-matched targeted therapy option available as of today in the second-line setting after progression on osimertinib, I think the most effective regimen is MARIPOSA-2 regimen. Well, this has been a great discussion. Our time is up. Thank you for listening. Thank you very much.

Announcer:
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