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Routes Reconsidered: A Case-Based Debate in SERD Selection

Dr. Jhaveri:
This is CE on ReachMD and I'm Dr. Komal Jhaveri.

Dr. Curigliano:
I am Giuseppe Curigliano. I work at the European Institute of Oncology in Milano and I will present a clinical case, a very special clinical case.

This is a 61-years-old woman. She was diagnosed in 2017 with a stage I disease. She received radiation therapy and finally adjuvant letrozole for an ER-positive, PR-positive, HER2 negative disease.

Unfortunately, in 2019, she had a local relapse, and so she started the first-line treatment with fulvestrant and palbociclib. During this treatment, she had a brain and liver progression. We performed a new biopsy in the liver, and we discovered an ER-positive, PR-positive disease, HER2 negative, and she received a dose of stereotactic radiation therapy of a right parietal lesion.

Unfortunately, during the treatment, she progressed and, sure, we started a second-line treatment with trastuzumab deruxtecan, but during the treatment with trastuzumab deruxtecan, she had an isolated progression of a brain mass. We performed the new radiation therapy and we moved her, finally, to a third-line capecitabine.

During capecitabine, she had again a brain progression. And so what's happening now, we performed a liquid biopsy. We discovered that there was an ESR1 mutation, and we started exactly elacestrant in combination with abemaciclib in the ELECTRA trial.

So surprisingly, during the treatment, while she was receiving the treatment, she had a responsive disease.

So I would like to get your opinion on this clinical case of the bioavailability of the drug in the blood-brain barrier and your impression on a late-line therapy with the oral SERD elacestrant.

Dr. Jhaveri:
So I think this is, again, a great example of the art that we can use in clinic, and we don't necessarily have to just follow each patient. I mean, of course, we use all the guidance and the level of evidence from trials to offer patients therapies, but certainly this is where we apply our clinical acumen and use that strategy to think about what if we did this and help our patients.

And we saw a little bit of that in the EMBER-3 study as well, that there is some brain metastases penetration for imlunestrant. And we know the ELECTRA trial with elacestrant is focused on the brain mets patient population.

Abemaciclib track record with brain metastases and even leptomeningeal disease, which is not a frequent thing in ER-positive cancers, but not completely unknown. We have patients with ER-positive tumors. So I would completely agree with your approach, and I'm very happy that your patient is doing really well on that strategy.

Dr. Curigliano:
But my question and my discussion with you, do you believe here the activity is more related to elacestrant or more related to abemaciclib in this patient?

Dr. Jhaveri:
Yeah. I think that's very hard to tease out, right? I think we know that abemaciclib certainly has more activity that we've been able to show, with more—I say more number of patients, if you will—that has been published with respect to brain metastases and the brain penetration and the leptomeningeal disease. With certain SERDS, we've seen some brain penetration preclinically, but we haven't seen a lot of clinical data. So we don't necessarily know that definitively, for single-agent outside of the EMBER-3 where it actually did that post hoc exploratory analysis, where we have some data that is published from that study. But we have ongoing trials like the ELECTRA trial trying to address these combinations, including in brain metastases population.

Dr. Curigliano:
I have only one final comment from you. Unfortunately, imlunestrant plus abemaciclib was not approved, but I personally believe this patient was an ideal candidate to that combination. Which is your impression on this?

Dr. Jhaveri:
Yeah, no, I think you're so right. I think our clinical unmet needs are so distinct from the regulatory approval paths. I think that's what it is, right? When we look at what we want for our patients in clinic, we very well know that we want majority of our patients to be treated with combination-based regimens, so we're very excited about data sets like EMBER-3.

Imlunestrant alone is approved. We don't yet have approval for the doublet. I'm hoping that maybe guidelines will start endorsing this and maybe the regulatory agencies will go back and now look at the doublet more closely now that they have settled the imlunestrant monotherapy approval and hopefully we can use that.

Dr. Curigliano:
Okay, we can conclude, I believe, Komal.

Dr. Jhaveri:
Yeah, absolutely. So I completely agree, that’s a wrap. We hope this case-based debate will be helpful in your practice. And thank you so much for listening in today.