2020 Target Therapy Forum

EGFR Question and Answer Panel

The Increase in Leptomeningeal Disease and the Connection with Mutation Positive NSCLC

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Dr. Jared Weiss: Good question, please address the increasing connection between EGFR and other mutations and the increase in leptomeningeal disease and how to treat it? I'll let you go first. I think I shared an experience earlier that came days after you gave your presentation, that was one of the two that led me to it. So I'll let you start with that since I'm already cited you.

Dr. Zofia Piotrowska: Well, thank you. I appreciate the shout out and, you know, I think this is a huge problem and such a challenge. It's such a hard thing to see in the clinic. And I think that the person was asking this question is right. We are talking more about leptomeningeal disease more than maybe we have in the past. I think for a few reasons, you know, I think one is that it seems that as these drugs get more potent and CNS penetrant, sometimes the types of resistance that we see, the types of progression that we see can become more challenging. Like for example, you know, patients who have done well on osimertinib when, when they progress, I don't know, actually if data, whether it's, you know, more common for them to progress on with leptomeningeal disease then on the older drugs. But it certainly is something that we see in the clinic. And it's a challenge.

It's a challenge because, you know, if someone has left them in jail disease before osimertinib, we know that osimertinib can be an effective strategy like you highlighted. But when that leptomeningeal disease arises on osimertinib, it becomes a lot more difficult to treat. And there is some, you know, evidence that chemotherapy can be helpful, pemetrexed, which has some brain penetration. Sometimes we use radiation as

well, but it's a real challenge. And it's something that's very, very difficult in the clinic and we need better treatments strategies for. As you alluded to, you know, doubling the dose of ghosts and osimertinib is something that we occasionally try for patients who are on 80 milligrams and develop leptomeningeal disease, sometimes we'll try going to 160, you know, the outcomes with that or that perhaps it might slow things down for a short period of time, but certainly not, you know, as good as we'd like it to be.

Dr. Jared Weiss: Yeah. I agree with absolutely everything you said. I passionately hate leptomeningeal disease. It trashes a quality of life. And for the most part we're really don't have great treatments for it. It's interesting that this question comes up in the context of EGFR and other mutations cause this is actually the first time we've been able to do anything effective about it. You know, I remember from training seeing patient after patient getting intrathecal methotrexate, and high dose methotrexate and, you know, people do these things and they just didn't work. I mean, there's something that, you know, tortures the patient without clear benefit, but in the targeted therapy or with these brain penetrating TKIs this is our first hope of actually really making a difference. If there's any association, I think it's that patients are living longer and having more time to get novel mechanisms of spread and novel problems.

Dr. Zofia Piotrowska: I would venture to guess that they're discussing the same topic and the ALK session and ROS1 session, for example, I don't know that it's something that's specific to EGFR. I just think that as these drugs are more effective and more brain penetrant, it's something that we're seeing more emerge.