



## **2020 Target Therapy Forum**

### **EGFR Question and Answer Panel**

# **Does Progression Always Occur on Osimertinib (Tagrisso) or is it Possible for it to Stop Cancer?**

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**Dr. Jared Weiss:** This is an important, basic question. Just progression, always occur on Tagrisso? Is it possible that it stops cancer?

**Dr. Zofia Piotrowska:** So that's such an important and great question. You know, I think the truth is that we expect that at some point cancers will progress on osimertinib. However, I will say that when that occurs is so hugely variable, and I think that the time that, you know, to development of progression can vary so much that there are patients that I've had in my clinic who've been on Tagrisso for years and maybe on Tagrisso for years. And I think what's really hard. And we saw this with older generations of EGFR inhibitors as well. And what's hard there is that, you know, we know that there's always this risk that we suspect that at some point, and, you know, even after a long time on a targeted therapy, when things have been going great, we expect that eventually the cancer may figure out its way around it. But there are patients whose disease remains controlled for such a long time that, you know, we hope that they will continue to be on that treatment. And I think often the longer you've been on a treatment, the better the chances that it will continue to work for a long period of time. And so it's a hard question. And I know for the patients who are asking, we always have this hope that this is going to be a drug that controls the cancer forever. And I think, you know, it's always something that we hope for. And at the same time, I think it's important to keep an eye out because we know that even after a long time it can develop.



Dr. Jared Weiss:

Yeah. I remember the first time I heard someone asked this question, because a formative experience on my pathway to becoming a thoracic oncologist cause that I will confess again, amongst you and a few of our friends, that it was not my first oncologic love. As a resident, I thought I was going to be a melanoma doctor cause I was so intrigued by immunotherapy at the time long before it was cool. Cause it was cool. I wouldn't do it. But I remember I was a resident across town from you. And I remember Tom Lynch coming across to BI and giving grand rounds on EGFRs. And he was asked that question and back when targeted therapy was so new, why doesn't it cure people? And I think that we've been that question has captured the attention of scientists and clinician scientists since the beginning. And while there are a lot of speculative answers we don't really have a solution for that. The sad truth is that resistance is inevitable in the overwhelming majority of patients.

But the optimistic counter note as you've noted is that we have patients who live extraordinary amounts of time with high quality of life and creative maneuvers, right? So you do your osimertinib, you do your osimertinib post progression. You use a little stereotactic radiosurgery, you switched to a chemo regimen. When after that maybe you come back to osimertinib and by the time you've done that, whatever resistance changed has become actionable on a trial. And, you know, as you string these things together, it's not just that you're keeping the person alive in that moment. All though that matters of course, but also that the science advances. And so, you know, if, when I see a newly diagnosed EGFR mutated patient and the question is, well, how long on average do you expect me to live? I don't know. And I have no clue for a very happy reason. I don't know just how insanely fast the science is going to advance and what creative maneuvers are going to work. But I will say that at least in my own head, my optimism is far greater than probably in the other class of patient that, with all of these maneuvers that the chance of a long lung survival is quite real.

Dr. Zofia Piotrowska:

I think that's such an important point and maybe such a hopeful note, I think, you know, to have at the end of the session is that, you know, really this is so true. If we look at the pace with which osimertinib went from phase one trials, which started, you know, 2011, 2012 to first FDA approval in the second line setting after T790M in 2015 to studies looking at it in the frontline setting to, you know, that being positive and to approval for frontline use in 2018, it's unprecedented. And if we look at the number of different drugs that have been improved for lung cancer, even this year, we are seeing that pace, I think, you know, becoming faster and faster for really great reasons. And I'm very hopeful and optimistic that we'll continue to see that and that we will have better treatments for patients, you know, who've already had osimertinib. And I think as you say that we will be able to come up with new ways to keep cancers and check on various treatments for a long, long time to come.



Dr. Jared Weiss:

So this has been really a great pleasure to present together with you and to chat with you. I want to briefly summarize for our audience and feel free to interrupt or add, but I think we've had an evolving standard in front-line that's really led us to osimertinib as the clear winner. We have numerous challenges, strategies of adding to it with VEGF and VEGF receptor agents bevacizumab and Ramucirumab or with chemotherapy. At the time of resistance, we have many strategies and the right ones to pursue is heavily dependent on the exact situation, a patient's physiologic strengths and weaknesses, and of course critically values, but they certainly include in our general arsenal treatment, past progression, stereotactic radiosurgery, as hamburger helper, if you will to keep our treatment working a little bit longer. Switch to chemo is about which regimen, continuation of drug with chemo returning to drug at some point later past progression. And that for our molecularly targeted effects we have a variety of resistance changes that emerge, great heterogeneity, and an emerging literature to lead us to believe that many of you are in fact actionable and will become increasingly actionable.

Dr. Zofia Piotrowska:

I think that's a great summary and you know, what I will add is that there's a lot of clinical trials in this space, you know, many, many ongoing around the country and around the world, and I'm sure many people on the line have already participated in those. And we are so incredibly grateful to them for, you know, contributing to those efforts and for, you know, working with us on these clinical trials. And I also encourage everyone to ask their doctors and, you know, to look into whether clinical trials maybe an option for them, because sometimes it can be a great way to access new treatments. That being said, for some patients it's not the right thing for various reasons. And that's okay too. There's lots of standard of care options that I think can be very effective. So I think, you know, hopefully we can end on a message of real hope and optimism for the future. And I know there's a lot of worry too, in COVID and the pandemic about whether we're still doing research and, and you know, whether we're still trying to advance the field. And I think it's also important to say that absolutely, you know, we are seeing patients with these types of lung cancers every day, and we know that this is just so incredibly important, and that, you know, new treatment strategies are needed and we will continue to work to develop them.

