Lung Cancer News and Updates ASCO 2020

Trial Updates-NSCLC

New Targets- MET and RET Positive NSCLC

New Potential Treatments for MET and RET Positive NSCLC: Capmatinib and BLU-667/Pralsetinib

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Dr. Jack West: Hi, I'm Dr. Jack West and I'm associate clinical professor in medical oncology at the City of Hope Comprehensive Cancer Center, and also the founder and president of GRACE, global resource for advancing cancer education. I'm very happy to be joined today for an ASCO highlights presentation in the field of lung cancer with two of my friends and colleagues from other parts of the country who are lung cancer experts with some different perspectives. And we're going to go through some of the key presentations and talk about what we think this means for patients. So first I have Dr. Helena Yu, who is medical oncologist at Memorial Sloan Kettering Cancer Center and Dr. David Spigel, who is chief scientific officer and director of the lung cancer program at the Sarah Cannon Cancer Center in Nashville, Tennessee. Thanks guys for joining.

It's been a very busy spring in 2020 in terms of new FDA approvals. And one of them was for a new agent against the target of MET, specifically MET Exon 14 mutations, which are in about two to 4% of patients with non small cell lung cancer. This agent Capmatinib now as the marketed name Tabrecta, and we knew it had good activity. We saw a little more data at ASCO, 2020 looking at cohorts of patients who got it either as a second or third line treatment and a smaller group on the right in the orange table who got it as first line treatment. And this is just more information that tells us what we already concluded, which is that this is a very active drug for patients with this target. If you identify it, you can also see that the response rates are clearly higher if these agents are given in the first line setting versus later.

And so, this is the data with Capmatinib, and you can also see that it induces good deep responses. And you can see part of the brain MRI of one patient is just really highlighting that many of these targeted therapies have good activity in the brain, both treating

brain metastases that exist, and also in usually, or hopefully preventing new brain metastases from developing in these patients. I put it's a different target, but a similar category. The drug pralsetinib is from blueprint medicines known as BLU-667 as well. This also had new data presented by Justin Gainer from Mass General, and we saw very good responses for patients with a RET fusion. This agent is not FDA approved, but there is another agent in this category targeting RET fusion called celpercatinib with very similar data.

And here you could see response rates of about 60%, and nearly every patient with at least disease control and then shrinkage of brain metastases here on the right, I'm sorry, on the left, you can see as so-called spider plot where downward trend over from left to right represents shrinking tumor. And there weren't a lot of patients to speak to, but seven of the nine patients who had measurable brain metastases had tumor shrinkage on this. And so these agents are now FDA increasingly FDA approved, pralsetinib hopefully soon, but we already have another one for RET fusion and it's exciting work. It's a new opportunity for a small population. I would say one of the challenges though, is that you're never going to find if you don't go looking for it, this is not, and these are the six seventh targets in a list.

And so I think that the only way that people are going to find these as if they do next generation sequencing, broad molecular testing, not one by one by one testing of a couple or three choice targets Helena, can you talk about a lot of this work's been done actually at Memorial. So can you talk about how transformative this is or how limiting it is if, you know, in terms of the challenges of next generation sequencing not being done necessarily in a timely way on a broad setting yet?

Dr. Helena Yu: Yeah, I mean, I think that as you mentioned, Jack, I think as we, you know, we're almost in the double digits with FDA approved drugs for these different targets, you'll never find something if you don't look for it. And I think if at all possible, I think with these really sort of incredible response rates and durations of response, if we can give these first line we really should try to give them first line. As we know with metastatic disease, some people don't get to second line and later treatment. So it's just so important to use the first treatment, the best treatment first, excuse me. And so I think, you know, the faster we get with next generation sequencing, if we can you know, have the results within two weeks, or if they get sent off earlier, that will be really helpful for our patients.

Dr. Jack West: David, anything to add, or do you know, you are working kind of on the interface, you have a pretty academic practice doing a ton of research, but you also work in a broader, you know, community setting for a lot of this research, how much, or how little of a barrier is this need for next gen sequencing to find these?

Dr. David Spigel: Well, I mean, not much to add, because I think the stories are so compelling. You know, these drugs are so effective, so active, you know, you'd go back to track even. I think people, many oncologists are recognizing that you're only going to find these if you test broadly and you just kind of get into a habit of doing it. And you know, it's not, it's not just this, right. I mean, there's TMB just got to be an approved strategy to use immunotherapy. What, last week? We talked about HER2. We didn't even talk about [inaudible] and Ross and ALK and EGFR to any great extent, but there's so many things we need to look for, you know, broadly testing makes sense. And so what we're seeing in our network are physicians talking more with their patients about this, and then trying to find the best way to do that for them.

And often it ends up being either sending tissue off to an outside laboratory to do that analysis or, and or blood to get back, at least a snapshot of some of those potential genetic alterations. So the main thing is, can you move somebody from not doing any testing to testing? And the answer is yes, it's happening everyday now, and then trying to help them understand what those results mean. And then how to use that to apply to a treatment, this kind of discovery, let's say you're a patient tomorrow, a doctor tomorrow with a patient, that might be your only patient with this kind of alteration for a year or two in the community. And so having experience is not going to be, you know, be easy for physicians. So this is going to be something that is going to take a lot of education and communication.

Dr. Jack West: But I also think that unfortunately, it's a setting where, you know, if you have a patient who you're doing NGS on everybody, if you find someone who's MET positive and you give Capmatinib and get a very good sustained response that not only is going to inspire you to keep looking for MET, but it will cross over to that same concept, applies for RET and TRECK and everything else. It's just, it doesn't, it's the same process and the same both testing process and thought process that applies from EGFR and ALK and ROS that we've been doing for a decade or more to these newer ones. It just, once you get beyond five and certainly approaching 10 or more targets, it only makes it more screamingly compelling. And I think now the scales have fully tipped to one side. And hopefully at this point it will be compelling enough that just about everyone will decide. We need to do whatever it takes to get this broad testing done.