Lung Cancer News and Updates ASCO 2020

Trial Updates-NSCLC

The SINDAS Trial-The Addition of SBRT to a Systemic EGFR (TKI) in EGFR Positive NSCLC

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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.

Another concept that I wanted to cover that was presented at ASCO 2020 is the integration of local therapies specifically in this case, adding radiation to systemic or whole-body therapy. This in the context of EGFR mutation positive advanced non-small-cell. We have seen in the last several years, a few relatively small studies of metastatic non-small cell that is with limited disease. And we will often turn that Oligoes Metastatic, oligoes, meaning few or few metastases that's often described as up to three or sometimes five spots of disease. So not people who have a lot of disease spread throughout their body, but in patients with very limited disease, there have been some small studies that have consistently shown better outcomes.

If patients got a combination of whole-body treatment with a good response, that was then followed by either surgery or more commonly radiation to areas of residual disease. And that is used selectively in some places I wouldn't call it a standard of care at this point, but this study comes out of China. It has 133 patients who had up to five spots of disease. And this is right from the time of starting treatment. It's a little

different from the design and some other studies because it didn't start with the whole body therapy, wait for a good response and then treat with radiation or surgery to just the leftover parts. This used an upfront approach of either the pill based therapy and of note. This was a first-generation EGFRs inhibitor, not quite as potent as the, the later ones that we use, especially Osimertinib Tagrisso, but it's still effective nonetheless.

So, you got this pill-based therapy, either alone or in combination with radiation it's called SBRT or stereotactic focal body radiation therapy, to all the sites of disease over just a few treatments. And then it looked at how people did. It looked at their progression free survival, how long before there was evidence that cancer was growing in places it was already present or new areas. And it also looked at survival. One point to make is that there is always in these studies [inaudible] from the entire pool of patients who might've been in it to a much smaller proportion, and here they started out screening 631 patients to get the 133 in the trial. It is important to note that this is always in an area where there is selection of patients.

And so, it's valuable to look at a randomized trial so that we aren't just looking at good results in patients who are doing well because they were eligible for the treatment. But what this study showed was a significant improvement in both progression free and overall survival. So with 30 to 40% improvement in how long patients went before their cancer was growing, as well as how long they lived. Now, this is not a huge study. And this study did not allow patients who had brain metastases. And this was not using the first line treatment that we would generally favor in the U S with Tagrisso. But I would say that it adds to a little more evidence that there is likely to be a benefit of adding local therapy to systemic therapy.

Perhaps particularly in the patients who have who have a systemic treatment that is likely to work very well, particularly targeted therapies for patients with a driver mutation, like EGFR could also apply to immunotherapy or chemo and immunotherapy, but I'm interested in your thoughts as well. Helena, I know that at Memorial you've integrated local therapies for some times, this isn't exactly new. What did you think of these data? Do you apply it very routinely or more selectively?

Dr. Helena Yu: Yeah, I think that as you mentioned, there are now several studies that have shown, you know, sort of variations of this strategy. And I think kind of it is a strategy in my opinion, that is probably underutilized that we don't always think about. I, you know, I think that there's this strategy, as you said, and then the strategy from the Gomez phase two study I sort of like the strategy of consolidating with local therapy and then.

Dr. Jack West: So, basically giving the local treatment as a chaser after getting a good response initially.

Dr. Helena Yu: Exactly. And I think that for me, I like that for two reasons. I think one is you're going to capture more patients. We actually had a study exactly like this, where we tried to find people that were all ago metastatic at presentation. And they're actually quite hard to find as you can see by sort of how the, the sample size of the study kind of winnowed down. And I also think that you get to get sort of a better sense of the natural history of the cancer, because I think if you see spore spots in someone when they're initially diagnosed you know, there could be a cult disease that you don't see that will blossom, you know, if they don't have an excellent response to treatment. So I think a couple of months in getting a sense to confirm, okay, these are the only sites of disease let's go after them after a good response.

And then I think you also make more people eligible. So people that might've had slightly more areas of involvement but if you get good and almost complete responses in some of them you'd be able to offer this treatment to them. But I mean, I think there's been several studies now that have shown a clear progression, free survival, as well as what's more important for this technique of course, is overall survival. Cause you're completely, you know, you're purposely getting rid of target lesions. So of course you are artificially you know, or sort of by very nature, improving progression free survival, but seeing, you know, an overall survival benefit in a few studies now I think is convincing enough for me to utilize this in my patients.

Dr. Jack West: So David, I'm sure you see patients with EGFR mutations or other drivers, but probably not in the same volume that I see on the West Coast or Helena at Memorial. And what, what's been your impression, you and your colleagues and Nashville in the last few years in the wake of these, some of these other smaller studies and how much, or how little does this add to that?

Dr. David Spigel: Yeah, well, I think, you know, we've been shifting in this direction, I think, as a field and maybe our colleagues in breast and colorectal cancer kind of led the way, but this idea of chasing down hotspots. And of course we all changed care well for a little while and limited stage small cell, you know, sorry, extensive stage small. So giving radiation after upfront chemotherapy, we didn't really understand why that would improve outcomes for patients when they have widespread disease. I use this strategy a lot, but I tend to wait. I tend to wait to be sure I'm not going to be surprised before putting someone through therapy that, you know, doesn't likely hit the main spots. And so until I'm sure what the cancer is I don't really go after them early. I also am unsure what is too many, you know, what is too many to go after? And I'm talking about outside the brain, cause we treat everything in the brain, but you know, is one lesion in the lung or several in a lung or several in the liver, just too many to do this with. And I had this study very

interesting. I think it's got a lot of false to it, but it's still, it's still interesting. And I think we're going to be seeing ourselves doing a lot more of this even beyond lung cancer.

Dr. Jack West: I agree. I also think it gets to a fundamental different concept. I was trained at a time when we were taught that metastatic is almost binary, it's like being a little pregnant or something. If you have metastatic disease, perhaps with the exception of one lesion that we called a precocious metastasis, there was not a value in giving local therapies like surgery or radiation to focus on one or two spots. If the so-called horse got out the barn anyway, there's no point locking the barn door after that. But this suggests that metastatic disease is more of a spectrum than a binary process. And that if you're on one end of the spectrum, that is more limited, even if it's not, even if it's still on the metastatic spectrum, you can potentially change the pace, the trajectory of systemic disease by treating with local therapy. I think that's a kind of fundamental change. And as you say, well, they are seeing data to support this in prostate and breast and some other settings. So I think it's a real change in how we think about it.

Dr. David Spigel: The one thing that we need and you know, I'd be interested know if Helena, you guys have saw this, as we do more of this over the last decade, you know, following people and knowing what scar or leftover effects versus progression can be troubling sometimes. And you know, I think technology with imaging is going to get better to help us discern what is actually viable tumor versus, you know, scar inflammation. Cause PET scanning is not good today. There not sufficient.

Dr. Helena Yu: Yeah, I think exactly. Right. And I think as we do this for more people or, or especially, I think it's relevant, I think for targeted therapy, it's easy to say you've treated the disease, but the treatment itself isn't so, you know, toxic. So we would just continue the targeted therapy, but I think it comes into play oftentimes with immunotherapy people who have excellent responses and we don't know what scar? What's residual disease and then treating it and then deciding whether or not to continue the immunotherapy. I think that's where it seems to come into play a lot too.