Lung Cancer News and Updates ASCO 2020

Mesothelioma Updates

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Dr. Jack West: Hi, I'm Dr. Jack West, 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.

Let's turn to mesothelioma cancer of the lining around the lung where chemotherapy typically cisplatin and Alimta or Pemetrexed, is a standard of care. Sometimes carboplatin with the cisplatin, are not great candidates for the cisplatin. And sometimes we add Avastin, the anti angiogenic, or blocking the blood supply agent along with the chemotherapy, there was a European study that showed a benefit, but it isn't FDA approved for that. It's not extremely widely used. Immunotherapy has been looked in this setting previously treated patients with mesothelioma after chemo and in trials like this, a little bit of data concurrent with chemotherapy. And here this was a study of 55 patients in the US presented by our colleague Patrick Ford at Johns Hopkins.

And so, it was cisplatin pemetrexed with Dirvalumab imfinzi and then maintenance Dirvalumab. And we see a median survival that is encouraging at 20.4 months. That again, media meaning half the patients are alive. And half have died by that time. For context in the larger phase three studies such as with bevacizumab, you tend to get around or just beyond a year and a half. So it's in that ballpark, but we also tend to see better results in these smaller studies than larger ones. So hard to get a sense of whether this is anything meaningful and I'm interested. Helena, can you give your thoughts about how provocative, these are to you, do you think this is likely to

translate to any change in management or is this comparable to what we can get everyday with the tools that we have?

Dr. Helena Yu: I think exactly, as you said, I think with a phase two study, it really is hard to make any definitive statements. You know, the dreamer study is already looking at this combo in the phase three setting in a randomized chemo versus chemo plus Dirvalumab. So I think that should be definitive in a way that this one was not. And then I think the other thing I think to note, and talking about it with some of the other abstracts we discussed there was sort of a notice from BMS that the IPI nivo study here was a positive study for whatever that means. And so I think another kind of challenge with the way that data comes out is, you know, will there be a different standard and how to sort of do that sort of cross trial comparison. So I think that'll be an interesting challenge. We'll look forward to the IPI nivo data.

Dr. Jack West: And David, how optimistic are you about this line of work? Is this exciting to you or do you think this is relatively less so for a phase two study?

Dr. David Spigel: You know, I don't know. I mean, I think there's just, there's limited things you can say here, but you know, I, it's funny just today we were, we had a chance to review Patrick's Dreamer study and we discussed, you know, what would change when we, you know, when we see the nivo Ipi data. And so, is this is a study going to finish? Is it going to, you know, are we going to have two options? So, I guess the main thing is even with bevacizumab, advantages what a few years ago, we really haven't seen any real shift in the care of Mesothelioma. So hopefully something will work. I just don't think there's much more, we can say beyond, beyond what you've commented on in this small study.

Dr. Jack West: And what do you do outside of a trial? Are you routinely incorporating Avastin bevacizumab, if you can, or do you have mixed feelings about that [inaudible]?

Dr. David Spigel: To be honest, outside of a study, I just, I tend to give just platinum pemetrexed routinely. I mean, I don't, I don't really use bevacizumab in that setting.

Dr. Jack West: And Helena, I don't know if you see very many of these old patients where you are?

Dr. Helena Yu: I really don't. But I agree with David that I think it seems like the standard for most is to just use the chemotherapy.

Dr. Jack West: Excellent. Staying on the theme of mesothelioma another trial that was interesting looked at treatment after first line therapy. And this was a study that looked at chemotherapy with gemcitabine, gemzar, which has been around for decades and has been a kind of secondary choice for mesothelioma before we routinely used Alimta pemetrexed, gemzar, was pretty commonly used in this setting. And it tends to be well tolerated. And this was a study for 164

patients included, enrolled who had already received chemotherapy, but didn't receive bevacizumab, Avastin, the anti-angiogenic or blood vessel supply drug.

And patients received either gemcitabine alone or in combination with, Cyramza also known as Ramucirumab, which is another antiangiogenic agent given IV. And patients were treated with one or these two drugs until progression or toxicity issues, with overall survival as the primary endpoint. And here you could see the progression free survival was nearly doubled in terms of median progression free survival, in the arm that got the combination, but it is not a statistically significant. And when we look at overall survival, you can see an improvement with the combination, and doesn't quite meet statistical significance, but a clear separation in these curves.

And when you look at the absolute difference in how many patients are alive a year in, and these are again previously treated patients, yeah, 56%, more than half on the combination and just a third who got the placebo arm of this study. And interestingly, we saw that there's a much more pronounced difference actually seen in the patients over 70 there's is not a large study, so it's not large numbers of patients, but it's interesting to see that the differences are actually most pronounced in the older patients. And yeah, so they did an analysis of a few different variables, but I don't want to get too far into the weeds when you know, it's not a large study.

This is not likely to lead to an FDA right now for no significant difference, but how intrigued are you by this? You stated that you're not necessarily enthralled by bevacizumab Avastin in the first line setting. Does this hold much merit or is this kind of more of the same? And not quite enough to emerge as a strong option for patients motivated for further treatment. Particularly when immunotherapy may also be an option that people are thinking about, whether it's on trials or off trials in mesothelioma where it's not FDA approved, but there's some activity there. Helena, can I start with you understanding that you have other people at your center who kind of eat, sleep, live and breathe mesothelioma and you don't?

Dr. Helena Yu: I mean, just looking at this data objectively as a little bit of an outsider. I mean, I think knowing mesothelioma, there really are not great second, third line options. And so I think that any improvement on the standard of care seems like, you know, at least a modest advance. And so I think if someone were to give gemcitabine or plan on giving gemcitabine, I think it is reasonable to add in the ramucirumab, I don't know if you would get sort of approval to do so at this time, but I think that the. And I think you might not have mentioned, but it seemed like the data or the benefit was irrespective as to whether the person got bevacizumab in the first line setting. So I think you know, it seems like a reasonable later line option.

Dr. Jack West: Is this something you would push for David or really not enough?

Dr. David Spigel: Well, I, you know, this study caught my attention. This was an odd trial, right? A small phase two study relative phase small study, but with an LS primary endpoint. So they were pretty ambitious here to, you know, pull off a positive study and they technically did that. I mean, they just missed it, I guess, with the P value, but they had a pretty nice hazard ratio. So, I think, you

know, it's just not going to be enough to change care, but I got to tell you, off study, I feel better about recommending Ram here than I do in my patients with non small cell lung cancer, where it's actually improved.

Dr. Jack West: Really? Cause the magnitude is greater?

Dr. David Spigel: Well, and we don't have many good options.

Dr. Jack West: Yeah. I'm not sure we have tremendous options after the chemo immunotherapy either, but anyway, it's good to see research being done in mesothelioma and curves that are separating, encouraging results.