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Guidelines-recommended first-line treatment with immunotherapy-based regimens in PD-L1- positive metastatic NSCLC

### Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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### Dr. Paz-Ares:

This is CME on ReachMD, and I'm Dr. Luis Paz-Ares.

### Dr. Yu:

And I'm Dr. Helena Yu.

### Dr. Paz-Ares:

For patients with PD-L1-positive metastatic non-small cell lung cancer, immunotherapy with or without chemotherapy is the standard first-line treatment.

Helena, what data support the guidelines for the use of immunotherapy in non-squamous non-small cell lung cancer?

### Dr. Yu:

Yeah, Luis, I think there are the seminal studies in the last 10 years, really, that have changed our first-line treatment for non-small cell lung cancer. So, really, the big studies in the non-squamous space are the KEYNOTE-189 study, which of course was the chemotherapy with or without pembrolizumab, really showing a marked improvement in both overall survival, hazard ratio of 0.6, and progression-free survival, 0.50. And we did see updated 5-year data really just showing that survival benefit is maintained over time.

And so for patients that have PD-L1 expression sort of agnostic, so 0 up to 100%, you could consider KEYNOTE-189. I think many of us focus for patients with PD-L1 expression greater than 50%. We focus on the data from KEYNOTE-024, which took patients with PD-L1 expression greater than 50% and randomized them to pembrolizumab versus chemotherapy. And that, again, really showed consistent overall survival benefits, a hazard ratio of 0.63.

And then I think that there are also data that suggest what if we intensify care? So one of those ICI/ICI plus chemotherapy regimens is the [CheckMate] 9LA study, which took patients and gave them ipilimumab, nivolumab, and 2 cycles of chemotherapy versus 4 cycles of chemotherapy, and that also showed a clear hazard ratio benefit, and that might be a regimen we can talk about when we would consider that, but for potential high-risk patients or with high tumor burden.

Luis, can you give me an overview of the data that support the guidelines for use of immunotherapy in squamous non-small cell lung cancer?

### Dr. Paz-Ares:

Of course, Helena. I think, actually, the data in the squamous cell lung cancer and metastatic disease are actually very similar to those in the non-squamous spaces. We have brain METs or palliative trials to those that have been done in non-squamous, or in some cases,

those trials have include the squamous non-small lung cell patients.

So the trials that at very time we have indication for immunotherapy as single agent for a patient with high expression, more than 50%, and that is based on trials such as KEYNOTE-024 or 042. In addition, the cemiplimab data also suggests similar benefit, or even the IMpower110 trial is also showing benefit in this very setting.

For those patients that do have tumors with PD-L1 less than 50%, that means 1% through 49% or less than 1%, we have data with different chemotherapy combinations, typically with carboplatin plus paclitaxel or nab-paclitaxel with different immunotherapies such as pembrolizumab. We have data as well with other agents such as cemiplimab, and on top of that, we have the data you have suggested with dual immunotherapy ipi/nivo plus or minus chemotherapy. And depending on the patient, we have a number of alternatives here to choose. Important to say you look at this long-term survival data; maybe for those patients that are PD-L1 negatives, and they maybe have some specific genomic aberrations such as KEAP1 or LKB1 mutations, some of those dual immunotherapy combinations may be a reasonable alternative.

**Dr. Yu:**

Absolutely. Those patients, maybe the risk, the added toxicity really is okay because there could be a potential benefit, and we know that patients with STK11 and KEAP1 really don't have robust responses to standard therapy.

Well, this has been brief but a great discussion. I hope we gave you something to think about and thanks for tuning in.

**Announcer:**

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