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https://reachmd.com/programs/cme/highlights-from-singapore-on-immunotherapies-in-metastatic-nsclc/16128/

Released: 09/25/2023
Valid until: 11/15/2024
Time needed to complete: 39m

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# Highlights from Singapore on Immunotherapies in Metastatic NSCLC

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**Dr. Aggarwal:**
Hi, I'm Dr. Charu Aggarwal. I'm here to discuss updates from the recent World Conference in Lung Cancer, and we'll discuss a few updates on immunotherapy and metastatic non-small cell lung cancer. I'm joined here by Dr. Forde, who will introduce himself.

**Dr. Forde:**
Hi. I'm Dr. Patrick Forde, a Medical Oncologist from the Thoracic Oncology Program at Johns Hopkins. I'm very happy to be here today.

**Dr. Aggarwal:**
Great. So we'll lead off with the first of the few studies that we're going to discuss. CheckMate 227 was one of the first studies, almost one of the initial studies I want to say, in the setting of metastatic non-small cell lung cancer long back in the day, where the study tried to evaluate the role of first-line immunotherapy or immunotherapy combinations, that is PD-L1, PD-1 blockade, along with CTLA4 blockade in patients with metastatic non-small cell lung cancer. Well, this has - the study has led to approval of nivolumab and ipilimumab in the metastatic setting for patients with PD-L1 greater than 1%, and is incorporated in clinical practice by many of us.

At this year's World Conference, we heard data from the 6-year follow-up as well as the 6-year update on this trial. What we saw was that with the use of dual immunotherapy checkpoint blockade, there was durable benefit on overall survival and duration of response. Actually, regardless of PD-L1 expression, there was greater tumor reduction seen, and there was association of long-term overall benefit. You know, even with the 6-year update, we did actually see a lot of new safety signals in large. And we've obviously had a lot of success in managing our AEs over time. How do you use these data, Patrick, in your practice? Are you more likely to use it or not?

**Dr. Forde:**
Yeah, we have. Historically, we were involved in quite a few of the early trials of CTLA4, PD-1 combination, and I think it is a regimen we use predominantly for PD-L1-low or negative disease. It's in the NCCN guidelines for PD-L1 negative disease, albeit only FDA approved for PD-L1 1% or above. I think the putative benefit here over PD-1 alone is this durable response from CTLA4 blockade. And we do see this I think at 6 years here, anything from 16 to just over 20% of patients had a continued benefit. And I think that's when we think historically 10 years ago of those figures, we would have been astounded, you know. So I think these long-term data are reassuring, both in terms of toxicity and also showing that some patients continue to derive benefit.

**Dr. Aggarwal:**
Absolutely. And in the same vein, we saw updated data, 5-year overall survival data from the pembrolizumab clinical trials, this time, specifically in the PD-L1 less than 1% or the PD-L1 negative category. Patrick, both you and I have, you know, sort of questioned what is the best approach for these patients? Because we know that historically, they don't tend to do well. Trial after another, we see that these overall survival rates don't quite meet the ones that are PD-L1 high positive or even intermediates. So what this presentation did

was they looked at pooled analysis from KEYNOTE 189 as well as 407, and evaluated outcomes with the use of chemotherapy plus pembrolizumab, specifically in patients with PD-L1 less than 1%. And what they reported on was 5-year overall survival of 12.5 percent with combination chemo versus only 9.5 percent with chemotherapy alone. I think with the hazard ratio of 0.64, very reassuring that if I were to choose this regimen on a patient, I think getting a 5-year survival of over 10% is actually quite gratifying, in my opinion. There were again, you know, overall response rate was in the order of 45 to 50%. And no new AE profiles, as well as, you know, a substantial number of patients were able to complete 35 cycles, complete the 2 years, come off therapy and, you know, be alive and included in the long-term follow-up. Your thoughts?

**Dr. Forde:**
I agree. And I think it reinforces the fact that in this PD-L1 negative population in the absence of targetable oncogene, PD-1 plus chemo is still the reference standard. And I think we were talking previously about moving ADCs into the first line setting and I think these are the sorts of long-term data that we'll be, when we're developing new drugs, we'll be trying to improve upon.

**Dr. Aggarwal:**
Absolutely. Again, very, very reassuring to see long-term follow-up of these trials. Another trial that was presented was the IMpower151 trial. This is a trial that incorporated atezolizumab into the treatment paradigm. And as you may remember, this is the trial that looked at combination of bevacizumab plus chemotherapy with atezolizumab. Unfortunately, it did not meet its primary endpoint of investigator-assessed PFS and the intent-to-treat population and the hazard ratio was only 0.84, but there were numerical improvements in progression-free survival. This trial showed that, you know, overall this regimen is well tolerated. No new safety signals again identified with this quadruplet; however, you know, I think as we saw in IMpowr150 using carboplatin, paclitaxel, atezolizumab, and bevacizumab, there may be certain subgroups of patients that do benefit, including EGFR and ALK. Although we should be cautious that those are subgroup analyses. I think another trial to show that it's safe to administer this combination, but again, may not be a homerun.

**Dr. Forde:**
I agree. I agree. I think we've been struggling to a degree to find the right population for this regimen, four-drug regimen. And I think this is one more study looking perhaps at a more tolerable treatment in terms of pemetrexed based compared to taxane. But again, no dramatic advance in this trial, I think, compared to what we have had previously available.

**Dr. Aggarwal:**
Great. Thank you for joining me, this was a great summary, and we look forward to more data in the future and more conferences. Thank you.

**Announcer:**
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