Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/keeping-pace-lung-cancer-role-immunotherapy-after-disease-progression/11724/

Released: 07/14/2020
Valid until: 07/14/2021
Time needed to complete: 15 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Keeping Pace: The Role of Immunotherapy After Disease Progression

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Keeping Pace: The Role of Immunotherapy After Disease Progression” is provided by Prova Education and is supported by an independent educational grant from Bristol Myers Squibb, Lilly, and Merck.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the Learning Objectives.

Dr. Socinski:
While advanced non-small cell lung cancer remains incurable, changes in treatment and new insights into the molecular pathogenesis of the disease have led to development of treatments that significantly extend overall survival. New scientific and clinical data have emerged on the role of immunotherapy after disease progression. How will these newer therapeutics be utilized in everyday clinical practice? This is CME on ReachMD, and I’m Dr. Mark Socinski.

Dr. Garon:
And I’m Dr. Edward Garon.

Dr. Socinski:
So welcome, Eddie. So let’s get started. So with ASCO just wrapping up, you know, I’d like to know what kind of caught your eye related to the immune checkpoint inhibitors in the first-line setting, and really get your comments on the updated analysis of KEYNOTE-189.

Dr. Garon:
So there was an update of the KEYNOTE-189 study at ASCO this year, and one thing that’s a bit unusual about the KEYNOTE-189 study is that the study was actually read out at its first interim analysis. So, at the time that it was read out, even though the study design required that patients receive pembrolizumab for a total of two years on the pembrolizumab arm, nobody on the study had made it really more than 21 months. And so, as a result, at the time that the data was presented, the follow-up was really quite immature. And so I think there were questions at this year’s ASCO as to when we looked at the final analysis from KEYNOTE-189, whether or not the sort of strongly beneficial outcomes with respect to progression-free survival, overall survival, and the benefits being distributed fairly evenly amongst patients who had no PD-L1 expression, PD-L1 expression in 1 to 49% of their cells, and PD-L1 expression in 50% or greater of their cells in the tumor would really be maintained as one looked over time. And in many respects, the outcome of this analysis was reassuring in that it was not surprising. What was found in this updated analysis with more mature follow-up is that, in fact, the overall survival and progression-free survival data that had been seen at the initial presentation and publication of this data, was maintained. The overall survival, progression-free survival was similar to what was seen at that early time point. In addition to that, there really did not seem to be a huge difference, at least with respect to the hazard ratios, amongst patients who had no PD-L1 expression, those with lower levels of PD-L1 expression, or those with higher PD-L1 expression.

I know, Mark, you also had some updated data from the IMpower150 study.

Dr. Socinski:

So, you know, we updated at the AACR meeting this year. It was the final overall survival analysis for IMpower150. As you remember, IMpower150 took the other standard regimen – actually the FDA-approved regimen of carboplatin, paclitaxel, and bevacizumab, the old ECOG 4599 data, and took two strategies. The first strategy was adding atezolizumab to the triplet regimen. So it was really looking at the interplay between anti-VEGF inhibition and anti-PD-L1 inhibition. And then a third arm that substituted atezolizumab for the bevacizumab. What we showed in the final analysis at AACR with regard to overall survival – that it was really the four-drug regimen, kind of the contribution of both atezolizumab and bevacizumab, that led to superior progression-free survival as well as overall survival. And relative to the direct comparison of bevacizumab and atezolizumab, there was no difference. Now, we would accept that adding bevacizumab, based on ECOG 4599 as well as other trials, has a survival benefit in that particular setting. This just confirms that, I think, there are two active components in the four-drug regimen in addition to chemotherapy. Now because there was some previous data suggesting that bev may have a delaying or a preventing effect on brain metastasis, we did a purely exploratory analysis that was presented at ASCO, and for those of you who are interested, it was abstract 9587. The suggestion there was that there did seem to be a delay, not necessarily a reduction in brain metastases, but a delay in the appearance of brain metastasis on the bevacizumab-containing arms of IMpower150. So seemingly was consistent with prior studies that were done, and so that was an interesting observation. But I would clearly note it as exploratory at this particular point.

So Eddie, one of the new bits of data – and we've had a couple of FDA approvals over the past month – has been the data that we saw with the non-chemo combination of nivolumab and ipilimumab, both CheckMate -227 and CheckMate -9LA, and I'd like to get your perspective on those two trials.

Dr. Garon:
We actually have now received FDA approval for a couple of regimens that involve nivolumab and ipilimumab. There was an update at this meeting from the CheckMate -227 study. This study was originally reported last year and evaluated a combination of nivolumab and ipilimumab and compared that to standard frontline chemotherapy. And what that study showed was that there did appear to be improvement, certainly, when one used the nivolumab and ipilimumab combination in that setting as opposed to chemotherapy. This data was updated at ASCO and the benefits that were seen – were maintained. They also, for the first time, presented data on another approach that would involve ipilimumab along with nivolumab, and in this case, patients would receive two cycles of chemotherapy in addition to the dual checkpoint inhibition. And the idea here was to address the fact that there are some patients who have been found, for instance, to have a hyperproliferative effect with immune checkpoint inhibitors. And in addition, there can be a delay of the benefit of immunotherapy, and perhaps a couple of cycles of chemotherapy would control the disease until immunotherapy could subsequently be of benefit. In the CheckMate -9LA study specifically, it seems that the trade-off was adding the ipilimumab but getting rid of chemotherapy beyond two cycles. But of course, also in that positive staining group is a group for which pembrolizumab as a single agent is approved based on the KEYNOTE-042 study, and now there's an approval for atezolizumab as well in high PD-L1 expressing patients. So I think that it's certainly exciting. We now have all of these positive data sets, and now practitioners will choose what they're going to do amongst these options.

Dr. Socinski:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Mark Socinski, and I'm joined by Dr. Edward Garon. We're discussing recent advances in the treatment of non-small cell lung cancer and their applications to everyday clinical practice.

Eddie, what I want to do is make a transition to how to use these therapies in patients who have oncogenic drivers, specifically EGFR, ALK, and others. And what role – once you've kind of exhausted your TKI options, what role do checkpoint inhibitors play at the time of progression in these patients?

Dr. Garon:
So, we certainly know that the group of patients with these sort of traditional addicted oncogenes – at least EGFR and ALK genomic abnormalities – have not received the same degree of benefit from immunotherapy as patients who are wild-type for EGFR and ALK. Some of the issues are that, in many respects, this group has been excluded from clinical trials looking at immunotherapy. Although the reason they've been excluded is that in early trials, they often were not groups that benefitted, and that has led to this exclusion. I think that many of us do consider incorporating immunotherapy as part of the IMpower150 regimen in patients in that setting. There is promising data in that group of patients; there's still no FDA approval there. There also are a few efforts looking at at pembrolizumab added to chemotherapy or chemotherapy alone in this setting, as well as approaches looking to incorporate nivolumab. But in general, although there are responders that we have seen anecdotally, certainly, and they've been published, with respect to single immune checkpoint inhibition to date, I would say this is a place where we still struggle.

Dr. Socinski:
Well, that's great. This has been an incredibly valuable conversation. Before we wrap up, Eddie, any last-minute thoughts, some take-home messages you'd want our listeners to leave with?

Dr. Garon:
I think that the one take-home that for me is sort of an exciting thing is just to think about how different the post-ASCO discussion is now versus about a dozen years ago. And that although it is complicating to now have these multiple subgroups of patients that require different therapies, it is difficult to assess between the relative benefits of multiple therapies that are available. Compared to where we came from not so long ago, these are major advances. And although we still have a long way to go, I think that it's really an encouraging time for people who manage patients with lung cancer.

Dr. Socinski:
I would completely agree. Unfortunately, that's all the time we have for today. So I want to thank our audience for your participation. And thank you, Dr. Garon, for joining me and for sharing all your valuable insights. It was great speaking with you today.

Dr. Garon:
Thank you very much.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education and is supported by an independent educational grant from Bristol Myers Squibb, Lilly, and Merck.

To receive your free CME credit, or to download this activity, go to ReachMD.com/ProvaEducation. Thank you for listening.