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<https://reachmd.com/programs/cme/ici-combination-regimens-for-first-line-treatment-of-metastatic-escc/33028/>

Released: 03/31/2025

Valid until: 03/31/2026

Time needed to complete: 46m

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## ICI Combination Regimens for First-Line Treatment of Metastatic ESCC

### Dr. Ajani:

This is CME on ReachMD, and I'm Dr. Ajani. Today I'll be talking about immunotherapy plus chemotherapy in first-line metastatic squamous carcinoma of the esophagus.

So to begin with, we'll talk about KEYNOTE-590. This particular study was sort of unique because it had adenocarcinoma patients and squamous carcinoma patients. Adenocarcinoma were less than 300, but squamous were 548. In this study, the pembrolizumab was combined with chemotherapy versus chemotherapy alone. The primary endpoint was overall survival, particularly for high PD-L1 patients defined as more than CPS of 10 or higher.

And in terms of efficacy, the study was successful. Pembrolizumab and chemotherapy did better than chemotherapy alone in terms of median survival was 12.6 months versus 9.8 months for the control. And similarly, the PFS was also prolonged with the addition of pembrolizumab, and overall response rate was higher.

The next one I will talk about is CheckMate 648. This study was the largest one, with 970 patients. But the unique thing about this study, there were two experimental arms and only one control. The one experimental arm was chemotherapy plus nivolumab, and the other experimental arm was nivolumab plus ipilimumab, and the control was chemotherapy only. And the primary endpoint was overall survival for PD-L1-positive patients, CPS of 1 or greater, so slightly different than KEYNOTE-590.

So this study, nivolumab plus chemotherapy did better than chemotherapy alone, with a higher response rate, longer median overall survival of 13.2 months versus 10.7 months, as well as the PFS was slightly longer, but it was not statistically significant.

The last study of great importance is RATIONALE-306. This study had 649 patients with tislelizumab plus chemotherapy as the experimental arm, and chemotherapy alone as the control arm.

The primary endpoint was overall survival for PD-L1-high patients. Again, this is defined as PD-L1 CPS score of 10 or greater. So this study was kind of interesting because the median overall survival was much longer than other studies. Although, it's not easy to compare one phase 3 trial with another, but the median overall survival was 17.2 months compared to 10.6 months. The response rates were much higher in this study for both the control and for the experimental arm. The PFS was significantly prolonged with a hazard ratio of 0.62. And overall response rate was also much higher than other studies.

So let me just sort of put these three studies into perspective. All three studies succeeded in producing results for the experimental arms, so it kind of changed the landscape for the next group of patients that come to our clinic. We can consider one of these anti-PD-1 molecule and chemotherapy for our patients, and we don't really need to consider chemotherapy alone unless there is a contraindication for immunotherapy.

So our time is up, and I hope that you will be able to implement some of these results in your practice. Thank you.