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Emerging Evidence for Perioperative ICIs in Locally Advanced HNSCC

Announcer:
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Dr. Uppaluri:
This is CE on ReachMD, and I'm Dr. Ravi Uppaluri. Today, I'll provide a brief overview of emerging evidence for perioperative immune checkpoint inhibitors in locally advanced head and neck squamous cell carcinoma, or HNSCC.

So I'll first talk about KEYNOTE-689, which focused on locally advanced head and neck cancer patients, stage III, IV, and IVA of the larynx, hypopharynx, or oral cavity and some oropharyngeal p16-negative patients and p16-positive patients. These patients were then randomized to receive either standard of care therapy or neoadjuvant pembrolizumab, 2 cycles prior to standard of care surgery.

Patients in the standard of care arm then went on to receive radiation therapy alone or radiation therapy plus cisplatin based on pathology-directed findings from the surgical specimens.

Patients in the pembrolizumab arm received pembrolizumab plus radiation concurrently or pembrolizumab plus radiation plus cisplatin concurrently, again, based on pathology-directed findings of intermediate-risk or high-risk features. These patients in the pembrolizumab plus standard care arm also were then maintained with 12 additional cycles of pembrolizumab.

The primary endpoint of this study was event-free survival by blinded independent central review. Secondary endpoints included major pathologic responses and overall survival.

The key findings of KEYNOTE-689 are shown here. First, the arms were balanced, with the majority of patients in both arms representing oral cavity squamous cell carcinomas. An intriguing finding from this study was that the pathologic features show that there were reduced high-risk features at 32.5% in the pembrolizumab plus standard of care arm versus 44.4% in the standard of care arm. This ultimately led to reduced radiation and less chemoradiotherapy in the pembrolizumab plus standard of care arm.

The overall survival at this first interim analysis was not significant, with a hazard ratio and P value as shown here. But this was the first interim analysis, and per the statistical plan, additional review will be performed at the second interim analysis.

Importantly, with the primary endpoint of the event-free survival, this was shown to meet statistical significance as defined by the statistical plan at 3 different analysis populations of CPS 10 or greater, 1 or greater, or all participants.

The 1 or greater Kaplan–Meier curve is shown here, showing a significant difference at the 3-year landmark interval with a hazard ratio of 0.7 and the P value of 0.0014. The median event-free survival was nearly 60 months in the pembrolizumab plus standard of care arm versus 29.6 months in standard of care arm.

Pathological responses were significant in the pembrolizumab plus standard of care arm, as expected, with the findings shown here for major path responses and pathologic complete responses. In particular, I'd like to highlight the CPS 1 or greater population showed nearly 10% major path response and a 3% complete response in CPS 1 or greater population.

The adverse events were again balanced between the 2 arms at 44.6% and 42.9% of grade 3 or higher events in the pembrolizumab plus standard of care arm versus standard of care arm, respectively. There were higher rates of immune-related adverse events in pembrolizumab plus standard of care arm, as expected. These were mostly hyper- or hypothyroidism, which were managed satisfactorily.

The NIVOPOSTOP study was focused primarily on patients who were high risk based on completed macroscopic surgical resection. These are stage III or IV patients with high-risk pathologic features concerning for relapse.

These patients were then randomized to receive standard of care adjuvant cisplatin radiation postoperatively or nivolumab prior to radiation, nivolumab concurrent with radiation plus cisplatin, and nivolumab maintenance, as shown here.

The key findings here was a disease cutoff as shown here, with 30.3 months follow-up, was that the 3-year disease-free survival was 63.1% with the nivolumab plus the chemoradiation and 52.5% with chemoradiation alone, with the hazard ratio as shown here of 0.76 and a P value of 0.034. Adverse events were similar between both arms. There were fewer locoregional relapses with nivolumab plus chemoradiation compared to chemoradiation alone. The overall survival data were not significant at this initial analysis, and it requires more data.

In summary, this KEYNOTE-689 regimen represents a new standard of care in resectable locally advanced head and neck cancer. These data were published in New England Journal of Medicine, and the FDA has approved this regimen for patients with CPS 1 or greater score on the tumor. I'd also like to highlight this is a safe approach, especially in the neoadjuvant window, but does require continuous close monitoring by surgeons, but it was very reassuring to not see patients progress on this regimen.

Second, NIVOPOSTOP represents additional new adjuvant treatment intensification approach for newly resected, locally advanced, high-risk locally advanced head and neck cancer patients. We are continuing to await the publication of these results to fully analyze the data and acquire additional details.

Well, my time is up. I hope you found this overview useful. Thank you for listening.

Announcer:
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