Immunotherapy improves survival in metastatic or recurrent head and neck cancer

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Prof Barbara Burtness, Yale School of Medicine and Co-Director, Development Therapeutics Research Program, Yale Cancer Center, New Haven, US, study author. Credit: © European Society for Medical Oncology

Immunotherapy with pembrolizumab improves survival in patients with head and neck cancer that has recurred or metastasised, according to late-breaking results from the KEYNOTE-048 study reported at the ESMO 2018 Congress in Munich.

The current standard treatment for metastatic or recurrent head and neck cancer is platinum-based chemotherapy (5-fluorouracil (5-FU) with cisplatin or carboplatin) plus the EGFR inhibitor cetuximab. Around 35% of patients respond to treatment, which leads to a median survival of just over ten months.

The phase III KEYNOTE-048 study examined whether the anti-PD-1 monoclonal antibody pembrolizumab could prolong survival and slow cancer growth compared to standard treatment. KEYNOTE-048 enrolled patients with head and neck cancer who had not received prior chemotherapy or biologic therapy for recurrent or metastatic disease. Patients were randomly allocated in a 1:1:1 ratio to: 1) standard treatment with platinum-based chemotherapy (5-FU with cisplatin or carboplatin) and cetuximab (the control group); 2) pembrolizumab alone; or 3) a novel combination of pembrolizumab and platinum-based chemotherapy.

At ESMO 2018 researchers presented results on pembrolizumab alone compared to standard treatment in patients expressing PD-L1, a marker of immune activity, and on the novel combination compared to standard treatment in all patients regardless of PD-L1 expression.

In the first comparison, 301 patients received pembrolizumab and 300 patients had standard treatment, with median follow up of 11.7 and 10.7 months, respectively. The patient demographics and disease characteristics were similar between the treatment arms.

In patients with tumour and/or surrounding cells expressing PD-L1 (combined positive score [CPS] >20), overall survival was significantly longer with pembrolizumab (14.9 months) than standard treatment (10.7 months, hazard ratio [HR] 0.61, p=0.0007). Some 23.3% responded to pembrolizumab and 36.1% responded to standard treatment. Median response duration was longer with pembrolizumab (20.9 months) than standard therapy (4.5 months). There was no difference in progression-free survival between groups (HR 0.99, 95% confidence interval [CI] 0.75-1.29).

"Patients with PD-L1 expression live longer when they have initial treatment with pembrolizumab," said first author Prof Barbara Burtness, Yale School of Medicine and Co-Director, Development Therapeutics Research Program, Yale Cancer Center, New Haven, US.

The results were similar in patients with a lower cut point of PD-L1 expression (CPS >1). Overall survival was significantly longer with pembrolizumab (12.3 months) compared to standard care (10.3 months, HR 0.78, p=0.0086). Some 19.1% on pembrolizumab responded to treatment compared to 34.9% on standard chemotherapy. Median response duration was longer with pembrolizumab (20.9 months) than standard chemotherapy (4.5 months). There was no difference in progression-free survival between groups (HR 1.16, 95% CI 0.75-1.29).

In the second comparison, 281 patients received the novel combination of pembrolizumab and platinum-based chemotherapy and 278 received standard treatment, with median follow-up of 13.0 and 10.7 months, respectively. Patient demographics and disease characteristics were similar between treatment arms. Overall survival was prolonged with the combination (13.0 months) versus standard care (10.7 months, HR 0.77, p=0.0034). Response rates were 35.6% for the pembrolizumab combination and 36.3% for standard treatment. There was no difference in progression-free survival between groups (HR 0.92, 95% CI 0.77-1.10).

Side effects in the three treatment groups were as expected. Pembrolizumab alone was less toxic than standard treatment. Pembrolizumab combined with chemotherapy and standard treatment had similar toxicity.

Burtness noted that compared to standard care, pembrolizumab alone had a lower response rate and numerically shorter progression-free survival, but significantly longer overall survival. She said: "Pembrolizumab appears to prolong life even when the cancer continues to grow, suggesting that it should be a first line therapy in recurrent and metastatic head and neck cancer. Whether pembrolizumab is given alone or with chemotherapy may depend on PD-L1 expression and we are conducting analyses to answer this question."

Commenting on the findings for ESMO, Dr. Tanguy Seiwert, Head and Neck Cancer Programme Director, and Assistant Professor of Medicine at the University of Chicago Medicine, Chicago, US, said: "This is the first study to show superior overall survival over the decade-old standard of care, platinum-based chemotherapy and cetuximab, and establishes PD-L1 CPS as a valid marker for head and neck cancer that should be routinely measured in these patients."

But he added: "The challenge is that treatment benefit is not equally distributed but depends on a biomarker. Hence, PD-L1 CPS expression will likely inform our choice between the two new options—pembrolizumab alone, with a favourable side effect profile, and pembrolizumab combined with chemotherapy, which may be used in a larger group of patients. Higher PD-L1 expression is associated with more benefit but the exact cut points have to be determined, and individual patient characteristics will play an important role as well. Separate analyses are needed in patients who have tumours with low or absent PD-L1 expression, where there is potentially less benefit."

Regarding the need for further research, Seiwert said: "The usefulness of other biomarkers to select patients for treatment, such as tumour mutational burden, should also be examined."

More information: Abstract LBA8_PR 'First-line pembrolizumab for recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC): interim results from the phase 3 KEYNOTE-048 study' will be presented by Barbara Burtness during the Presidential Symposium 3 on Monday, 22 October, 16:30 to 18:00 CEST in Room 18 - Hall A2. *Annals of Oncology*, Volume 29 Supplement 8 October 2018

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