Oesophageal

Nivolumab Combination Therapy in Advanced Oesophageal Squamous-Cell Carcinoma

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BACKGROUND

First-line chemotherapy for advanced oesophageal squamous-cell carcinoma results in poor outcomes. The monoclonal antibody nivolumab has shown an overall survival benefit over chemotherapy in previously treated patients with advanced oesophageal squamous-cell carcinoma.

METHODS

In this open-label, phase III trial, we randomly assigned adults with previously untreated, unresectable advanced, recurrent, or metastatic oesophageal squamous-cell carcinoma in a 1:1:1 ratio to receive nivolumab plus chemotherapy, nivolumab plus the monoclonal antibody ipilimumab, or chemotherapy. The primary end points were overall survival and progression-free survival, as determined by blinded independent central review. Hierarchical testing was performed first in patients with tumour-cell programmed death ligand 1 (PD-L1) expression of 1.0% or greater and then in the overall population (all randomly assigned patients).

RESULTS

A total of 970 patients underwent randomisation. At a 13-month minimum follow-up, overall survival was significantly longer with nivolumab plus chemotherapy than with chemotherapy alone, both among patients with tumour-cell PD-L1 expression of 1.0% or greater (median, 15.4 vs. 9.1 months; hazard ratio, 0.54; 99.5% confidence interval [CI], 0.37 to 0.80; P<0.001) and in the overall population (median, 13.2 vs. 10.7 months; hazard ratio, 0.74; 99.1% CI, 0.58 to 0.96; P=0.002). Overall survival was also significantly longer with nivolumab plus ipilimumab than with chemotherapy among patients with tumour-cell PD-L1 expression of 1.0% or greater (median, 13.7 vs. 9.1 months; hazard ratio, 0.64; 98.6% CI, 0.46 to 0.90; P=0.001) and in the overall population (median, 12.7 vs. 10.7 months; hazard ratio, 0.78; 98.2% CI, 0.62 to 0.98; P=0.01). Among patients with tumour-cell PD-L1 expression of 1.0% or greater, a significant progression-free survival benefit was also seen with nivolumab plus chemotherapy over chemotherapy alone (hazard ratio for disease progression or death, 0.65; 98.5% CI, 0.46 to 0.92; P=0.002) but not with nivolumab plus ipilimumab as compared with chemotherapy. The incidence of treatment-related adverse events of grade 3.0 or 4.0 was 47% with nivolumab plus chemotherapy, 32% with nivolumab plus ipilimumab, and 36% with chemotherapy alone.

CONCLUSION

Both first-line treatment with nivolumab plus chemotherapy and first-line treatment with nivolumab plus ipilimumab resulted in significantly longer overall survival than chemotherapy alone in patients with advanced oesophageal squamous-cell carcinoma, with no new safety signals identified.