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### Pembrolizumab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced esophageal cancer: The phase 3 KEYNOTE-590 study

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## Background

KEYNOTE-590 (NCT03189719) is a randomized, international, double-blind study of 1L pembrolizumab (pembro) + chemotherapy (chemo) vs chemo alone in patients (pts) with locally advanced/unresectable or metastatic adenocarcinoma or esophageal squamous cell carcinoma (ESCC) or Siewert type 1 esophagogastric junction adenocarcinoma (EGJ).

## Methods

Eligible pts were randomized 1:1 to pembro 200 mg or placebo Q3W for up to 2 yr + chemo (cisplatin 80 mg/m<sup>2</sup> Q3W [d1; 6 doses] + 5-FU 800 mg/m<sup>2</sup> on d1-5 Q3W). Randomization was stratified by Asia vs Rest of World, adenocarcinoma vs ESCC, and ECOG PS 0 vs 1. Treatment continued until progression, unacceptable toxicity, or withdrawal, or 2 yr. No crossover was permitted. Primary end points were OS in pts with ESCC PD-L1 combined positive score (CPS)  $\geq 10$  tumors, and OS and PFS (RECIST v1.1; by investigator) in ESCC, PD-L1 CPS  $\geq 10$ , and all pts. The secondary end point was ORR (RECIST v1.1; by investigator) in all pts. Data cutoff for interim OS/final PFS analysis was July 2, 2020.

## Results

At data cutoff, 749 pts (83% male, 73% ESCC) were randomized (373 pembro + chemo; 376 chemo). Median follow-up was 10.8 mo. Pembro + chemo vs chemo was superior for OS in pts with ESCC CPS  $\geq 10$  (median 13.9 vs 8.8 mo; HR 0.57; 95% CI, 0.43-0.75;  $P < 0.0001$ ), ESCC (median 12.6 vs 9.8 mo; HR 0.72; 95% CI, 0.60-0.88;  $P = 0.0006$ ), CPS  $\geq 10$  (median 13.5 vs 9.4 mo; HR 0.62; 95% CI, 0.49-0.78;  $P < 0.0001$ ), and all pts (median 12.4 vs 9.8 mo; HR, 0.73, 95% CI, 0.62-0.86;  $P < 0.0001$ ). PFS was superior with pembro + chemo vs chemo in ESCC (median 6.3 vs 5.8 mo; HR 0.65; 95% CI, 0.54-0.78;  $P < 0.0001$ ), CPS  $\geq 10$  (median 7.5 vs 5.5 mo; HR 0.51; 95% CI, 0.41-0.65;  $P < 0.0001$ ), and all pts (median 6.3 vs 5.8 mo; HR 0.65; 95% CI, 0.55-0.76;  $P < 0.0001$ ). Confirmed ORR was 45.0% vs 29.3% ( $P < 0.0001$ ) in all pts, with median DOR of 8.3 vs 6.0 mo. Grade 3-5 drug-related AE rates were 72% vs 68%. Discontinuation rates from drug-related AEs were 19% vs 12%.

## Conclusions

Pembro + chemo provided superior OS, PFS, and ORR vs chemo, with a manageable safety profile in pts with untreated, advanced esophageal and EGJ cancer. These data demonstrate that 1L pembro + chemo is a new standard of care in this pt population.

## Clinical trial identification

NCT03189719.

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## Legal entity responsible for the study

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