## LBA – 005 KEYNOTE-061: Phase 3 study of pembrolizumab vs paclitaxel for previously treated advanced gastric or gastroesophageal junction (G/GEJ) cancer

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**Background:** Pembrolizumab showed promising antitumor activity and a manageable safety profile in patients with pretreated G/GEJ cancer in KEYNOTE-012 and KEYNOTE-059. KEYNOTE-061 (NCT02370498) was a global, open-label phase 3 study of pembrolizumab vs paclitaxel for previously treated advanced G/GEJ adenocarcinoma that progressed after first-line chemotherapy containing platinum and fluoropyrimidine.

**Methods:** Eligible patients were randomized in a 1:1 ratio to pembrolizumab 200 mg Q3W or paclitaxel 80 mg/m2 on days 1, 8, and 15 of 4-week cycles. Randomization was stratified by geographic region, TTP on first-line therapy, and PD-L1 combined positive score (CPS). Primary end points were OS (efficacy boundary, one-sided $P = 0.0135$) and PFS in the CPS $\geq 1$ population. Differences in OS and PFS were assessed using the stratified log-rank test.

**Results:** Of the 592 patients enrolled, 395 had PD-L1 CPS $\geq 1$: 196 assigned to pembrolizumab, 199 to paclitaxel. After median follow-up of 8 mo, 7.8% of patients completed or remained on pembrolizumab. Median OS was 9.1 mo (95% CI 6.2-10.7) with pembrolizumab vs 8.3 mo (95% CI 7.6-9.0) with paclitaxel (HR 0.82, 95% CI 0.66-1.03; one-sided $P = 0.042$). 12-mo OS rates were 39.8% vs 27.1%; 18-mo rates were 25.7% vs 14.8%. There was no improvement in PFS (median 1.5 mo with pembrolizumab vs 4.1 mo with paclitaxel; HR 1.27 [95% CI 1.03-1.57]) or ORR (15.8% vs 13.6%), but pembrolizumab responses were more durable (median 18.0 mo vs 5.2 mo; duration $\geq 12$ mo 59.5% vs 29.5%). The pembrolizumab treatment effect for OS was more evident in patients with ECOG PS 0 (median OS 12.3 mo vs 9.3 mo; HR 0.69, 95% CI 0.49-0.97). In post-hoc analysis, the pembrolizumab treatment effect for OS was also greater in patients with CPS $\geq 10$ (median OS 10.4 mo vs 8.0 mo; HR 0.64, 95% CI 0.41-1.02) and in patients with MSI-H tumors, regardless of CPS (median OS not reached vs 8.1 mo; HR 0.42, 95% CI 0.13–1.31). In all patients, grade 3-5 drug-related AE incidence was 14.3% with pembrolizumab vs 34.8% with paclitaxel; 3.1% vs 5.4% discontinued due to drug-related AEs.

**Conclusions:** Pembrolizumab did not significantly improve OS vs paclitaxel in patients with previously treated G/GEJ cancer and PD-L1 CPS $\geq 1$, although a benefit for pembrolizumab emerged with long-term follow-up. Pembrolizumab had a better safety profile than paclitaxel. The pembrolizumab treatment effect was more evident in patients with ECOG PS 0, those with greater PD-L1 expression, and those with MSI-H tumors. Trials of pembrolizumab as monotherapy and as part of combination therapy for G/GEJ cancer are ongoing.